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MAY 1951

VOLUME 45 NUMBER 5

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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A prism is a wedge shaped piece of glass, thicker at the base than at the apex by an amount that is determined by the following formula:

$$T = .0191 \times P \times D$$

In this formula "T" is the difference in thickness between the base and the apex. "P" is the prism and "D" is the diameter of the lens. The table below was computed from this formula and shows the thickness difference between the base and the apex of knife edge prisms. The table is figured for optical crown glass of index 1.523. For flint glass of index 1.690 multiply the figures given in the table by 0.758.

Prism	DIAMETER OF LENS					
	38	40	42	44	46	48
.5	.36	.38	.40	.42	.44	.46
1.0	.72	.76	.80	.84	.88	.92
1.5	1.09	1.15	1.20	1.25	1.32	1.38
2.0	1.45	1.53	1.61	1.68	1.76	1.84
2.5	1.82	1.91	2.01	2.10	2.20	2.30
3.0	2.18	2.29	2.41	2.50	2.64	2.76
3.5	2.54	2.67	2.81	2.92	3.08	3.22
4.0	2.90	3.05	3.20	3.36	3.52	3.68
4.5	3.26	3.43	3.60	3.78	3.96	4.14
5.0	3.62	3.81	4.00	4.20	4.40	4.60
6.0	4.34	4.56	4.79	5.00	5.28	5.42
7.0	5.05	5.32	5.58	5.84	6.16	6.44
8.0	5.76	6.10	6.37	6.72	7.04	7.36
9.0	6.46	6.80	7.14	7.56	7.92	8.28
10.0	7.17	7.54	7.92	8.40	8.78	9.17

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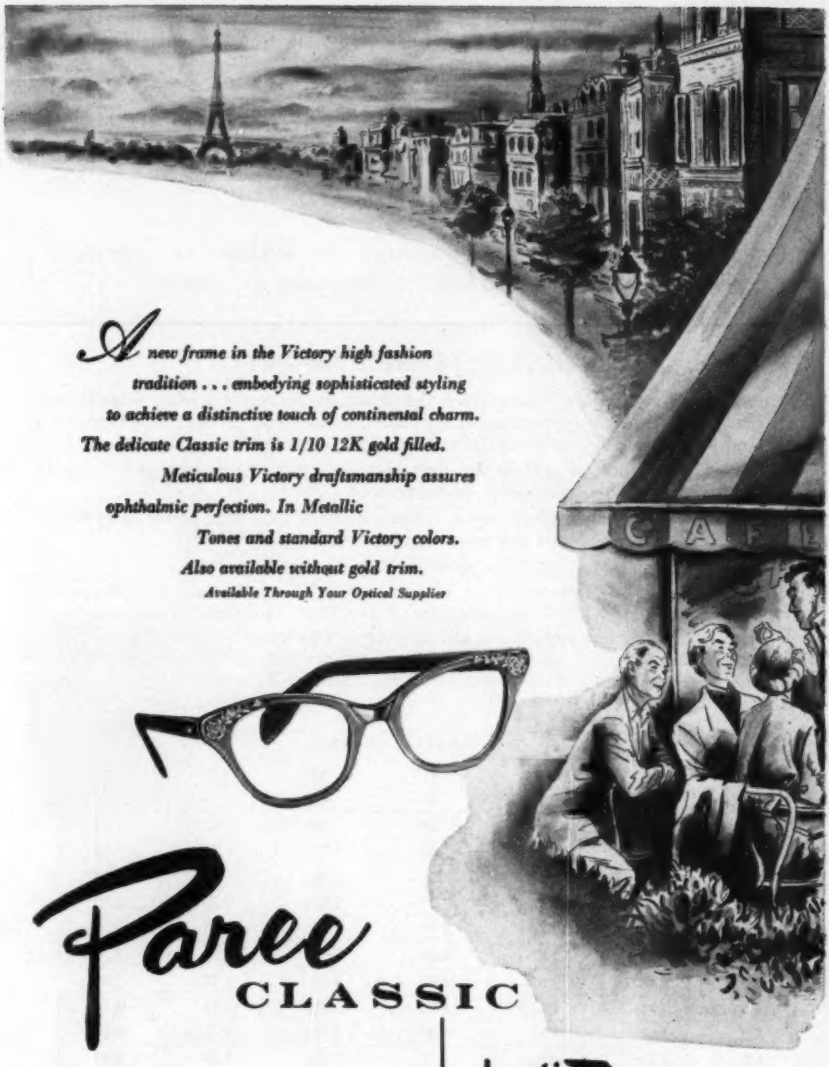

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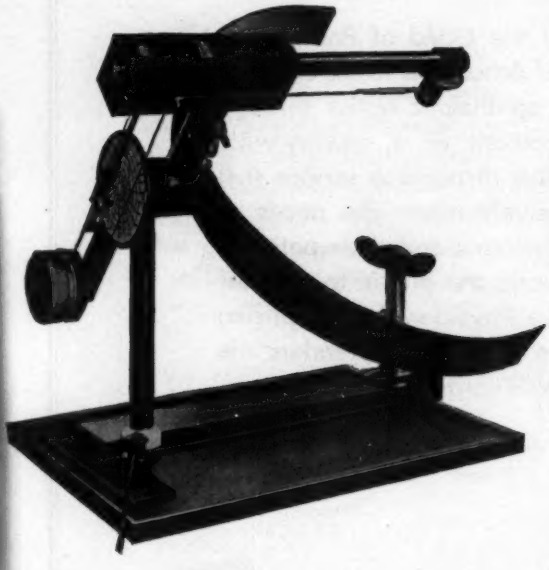

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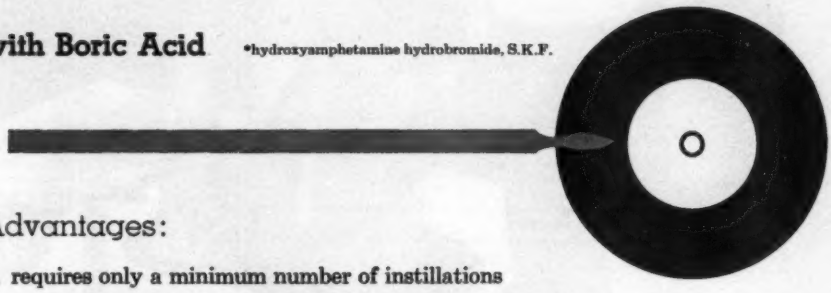

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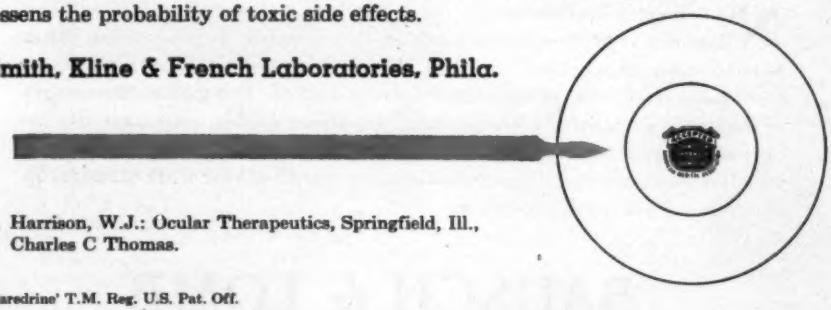

1. Harrison, W.J.: Ocular Therapeutics, Springfield, Ill., Charles C Thomas.

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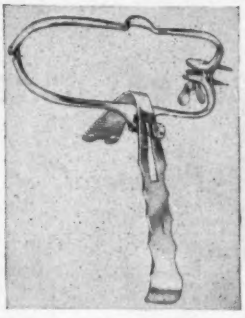

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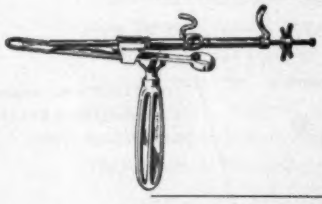

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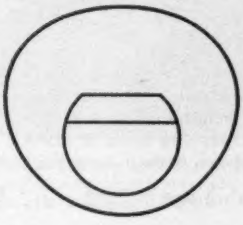

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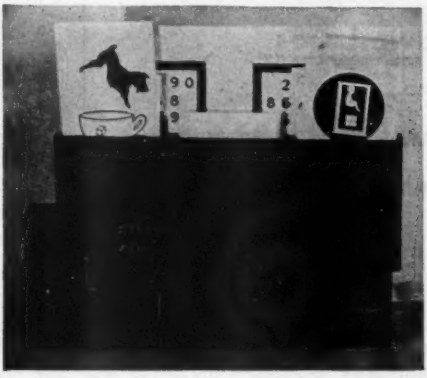

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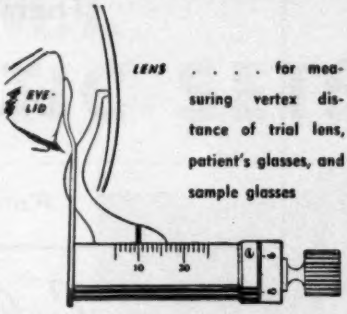

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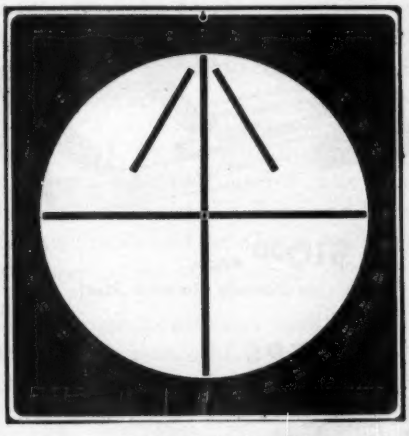

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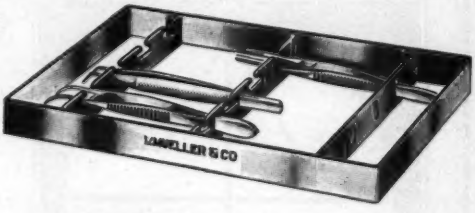

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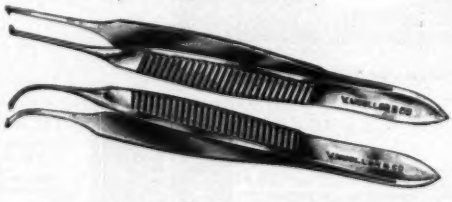

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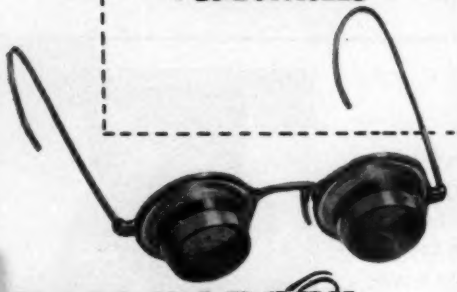

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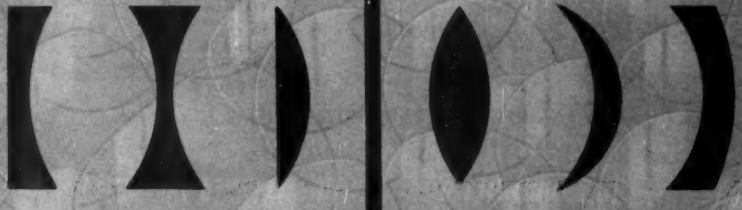

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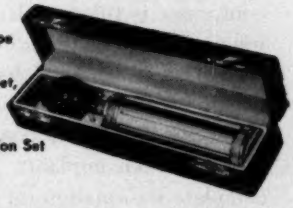

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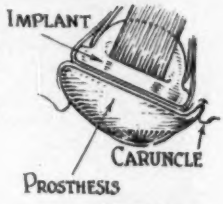

FIGURE 1

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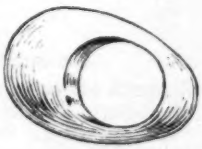

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VOLUME 45 MAY 1951 NUMBER 5

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Editorial

REGISTRY OF INTERESTING CASES

To many of us, and I dare say most, interesting cases are the spices of our professional lives. But they have to be shared to be appreciated. What many of us do on seeing such a case is confer with a colleague or two from across the hall and let it go at that, feeling that when the time is available we will "look it up." But time passes, and to look further than in the few texts on our personal shelves is no little chore. Hence it comes to be relegated to a variously obscure position in the storehouse of our memories to be called upon at some future time, if at all, with something short of accuracy.

Actually many unique cases are undoubtedly lost because there has been no filing system in which they may be conveniently deposited. To report a case has come to mean a review of the literature, a comprehensive study from as many points of view as seem remotely pertinent, and a discussion of related cases, with often a number of unrelated observations thrown in. While a thorough work-up is laudable when time and opportunity are available, it cannot be denied that it has its disadvantages as well, for it deters most of us who never get around to "look it up" from recording and sharing much of the interesting material we see. Besides, we are afraid of exposing our ignorance lest what is interesting to us is old-time stuff to our peers.

Accordingly, a new section is being started with this issue called "Registry of Interesting Cases" where no claim is made for priority, no necessary review of the literature is attempted, clinical investigation may or may not have been exhaustive, and discussion is limited to a minimum. Such reports need be no more than a few paragraphs stating only such facts as are necessary for the adequate description of the case with photographs where possible. An exact and specific title is of the utmost importance, for this is what will be cross referenced in the literature and provide the permanent value that the case reports will have. The cases submitted must necessarily be passed by the Editorial Board for concurrence in the interesting aspects of the case, and correspondence from the profession will be welcomed in reference to those published. In no sense does this supplant the clinical case reports or the presentation of syndromes, which will continue to be feature articles. It is simply an attempt to share on a larger scale the experiences and information which heretofore we have had only with our colleagues across the hall.

DAVID G. COGAN, M.D.

EXPERIMENTAL RADIATION CATARACTS

I. Cataracts in the Rabbit Following Single X-Ray Exposure

DAVID G. COGAN, M.D.
AND
DAVID D. DONALDSON, M.D.
BOSTON

RADIATION cataracts have been of interest as medical and biologic phenomena since the early days of roentgenology, when an unusual type of cataract developed in certain x-ray technicians without necessarily other manifestations of irradiation developing. This apparent predisposition of the lens has intrigued investigators not only because of its practical importance but also because, on a priori grounds, one would not expect a tissue having the slow rate of growth of the lens to be particularly susceptible to radiation.

Recent interest in the subject has been accentuated by the occurrence of radiation cataracts in cyclotron workers [1] and in some of the persons exposed to radiation from the atomic bomb.[2] Accordingly, the Committee on Radiation Cataracts was formed under the auspices of the National Research Council for the purpose of stimulating research in this field, and the work to be reported in this paper was supported by a grant from the Atomic Energy Commission on recommendation of the National Research Council committee.

The purpose of the present study was to obtain quantitative information on the cataractogenic dose from acute exposure to x-rays. It was, of course, recognized that acute exposures and the x-radiation did not necessarily simulate the conditions of exposure under which the cyclotron and atomic bomb cataracts developed, but it is presumed that the pathogenesis of the cataracts is the same whether the exposure is acute or chronic and irrespective of the type of radiation so long as it is from an ionizing source, i. e., x-rays, gamma rays or neutrons. The generalities that are established with x-ray cataracts may, therefore, be accepted for other types of radiation, and the difference in dosage will have to be determined by further experimentation.

Sufficient information is available on x-ray cataracts in human beings to indicate that the probable cataractogenic dose of x-rays of 100 kv. energy or greater is somewhere between 500 and 1,000 r [3] and that the younger the person, the

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and The Massachusetts Eye and Ear Infirmary.

1. Radiation Cataracts, editorial, J. A. M. A. **140**:1218 (Aug. 13) 1949. Abelson, P. H., and Kruger, P. G.: Cyclotron Induced Radiation Cataracts, Science **110**:655 (Dec. 16) 1949.

2. Cogan, D. G.; Martin, S. F., and Kimura, S. J.: Atom Bomb Cataracts, Science **110**:654 (Dec. 16) 1949.

3. Hunt, H. B.: Cancer of the Eyelid Treated by Radiation, with Consideration of Irradiation Cataract, Am. J. Roentgenol. **57**:160, 1947.

greater the susceptibility.[4] These observations on human beings are necessarily scanty,[5] and it will be one function of the present study to subject them to experimentation in rabbits. Suffice it to say that Desjardins,[4] who has compiled the most exhaustive résumé of the effects of x-rays on the eye, concluded that the lens of the mature eye was notably insensitive to radiation.

X-ray cataracts have been produced in rabbits on several occasions previously. In fact, they were reported in animals within two years after Roentgen's announcement of the discovery of x-rays.[7] Vacuoles and opacities occur in the rabbit lens beneath the posterior capsule,[8] as in the human lens, but equatorial changes are more evident in the early stages of radiation cataract of rabbits (Leinfelder and Kerr [4]). The dose necessary to cause cataract in rabbits has been reported to be of the order of 550 to 1,000 r [9] when 150 to 200 kv. x-rays are used; and the larger the dose, the shorter the latent period.[10] It is often stated, but without convincing evidence as yet, that the milder lenticular changes from irradiation are reversible.

Histological changes in the lenses following irradiation, as studied by means of cross sections [11] and flat preparations,[12] have shown vacuolation and degeneration in the cells, and the lens fibers have failed to show a normal arcuate differentiation at the equator.[11b] The chromosomes of the lens epithelial cells are said to become fragmented, and the nuclei disintegrate, producing a disorderly pattern of cells, often with multiple nuclei. These changes are similar to those that have been

4. There are numerous references in the older literature indicating a greater susceptibility of the young lens; these references were listed and discussed by Desjardins (Desjardins, A. V.: Action of Roentgen Rays and Radium on Eye and Ear: Experimental Data and Clinical Radiotherapy, Am. J. Roentgenol. **26**:643, 789 and 921, 1931). The most recent article pointing to the greater susceptibility of the young lens is that of Leinfelder and Kerr (Leinfelder, P. J., and Kerr, H. D.: Roentgen-Ray Cataract: An Experimental, Clinical and Microscopic Study, Am. J. Ophth. **19**:739 [Sept.] 1936).

5. Relatively recent reviews of radiation cataract in human beings are those of Rohrschneider, Mitner and Desjardins (Rohrschneider, W.: (*a*) Experimentelle Katarakt nach mehrfacher Bestrahlung mit kleinen Röntgenstrahlendosen, Ber. u. d. deutsch. ophth. Gesellsch. **48**:241, 1930; (*b*) Untersuchungen über die Morphologie und Entstehung der Röntgenstrahlenkatarakt beim Menschen, Arch. f. Augenh. **106**:221, 1932. (*c*) Mitner, J. G.: Irradiation Cataracts, Brit. J. Ophth. **18**:497, 1934. Desjardins.[4]

6. Footnote deleted.

7. Chalupecký, H.: Über die Wirkung der Röntgenstrahlen auf das Auge und die Haut, Centralbl. f. prakt. Augenh. **21**:234, 267, 1897.

8. (*a*) Peter, L.: Studien zur experimentellen Röntgen- und Radium Katarakt, Arch. f. Ophth. **125**:428, 1930. (*b*) Okusawa, T.: Die experimentelle Untersuchung über die durch Röntgenstrahlen verursachten Veränderungen des Linsenepithels, Acta Soc. ophth. Jap. **37**:814, 1933; abstracted, Klin. Monatsbl. Augenh. **92**:695, 1934. (*c*) Poppe, E.: Experimental Investigations of the Effects of Roentgen-Rays on the Epithelium of the Crystalline Lens, Acta radiol. **23**:354, 1942.

9. Leinfelder and Kerr.[4] Peter.[8a] Poppe.[8c] Rohrschneider.[5a]

10. Peter.[8a] Poppe.[8c]

11. (*a*) Leinfelder and Kerr.[4] (*b*) von Sallmann, L.: Report on Studies of the Effect of Roentgen Irradiation on the Rabbits' Lens, United States Atomic Energy Commission Declassified Document no. NYO-1508, April, 1950; abstracted, Nuclear Sc. Abstr. **4**:631 (July 31) 1950; Experimental Studies on Early Lens Changes After Roentgen Irradiation, Arch. Ophth. **45**:149 (Feb.) 1951. (*c*) Gredzielski, J.: Zur Histologie der Röntgenkatarakt, Klin. Monatsbl. f. Augenh. **95**:360 (Sept.) 1935.

12. Poppe.[8c] von Sallmann.[11b]

reported in other tissues after radiation.[13] In addition, cytochemical changes in the lens epithelial cells have indicated that radiation results in a reduction in the desoxyribonucleic acid and depolymerization of the acid in many nuclei.[11b]

The present study aims to test the validity of some of the foregoing observations with a sufficient number of rabbits and to add such new information as might be useful in elucidating the pathogenesis of radiation cataract. Especially emphasized, because sufficient information was considered to be lacking in the literature, were (1) the correlation of radiation cataracts with other manifestations of irradiation in and about the eye, (2) determination of the exact threshold for x-ray cataract in the rabbit and (3) a study of the variation in cataract formation throughout the entire life span of the rabbit. Finally, it was hoped to obtain an explanation of the curious localization of the initial opacities in radiation cataract in the posterior subcapsular regions of the lens.

The procedure differed from that previously employed in that most of the exposures were made with x-rays of 1,200 kv. energy. This had the distinct advantage of permitting the clinical study of the course of events in the development of the cataract with less clouding of the cornea than that which results and greatly handicaps the examination of the lens when x-rays of less energy are used.

MATERIALS AND METHODS

Chinchilla rabbits were used throughout,[14] and, except those used in the age study, all were within a few days of being 10 weeks old at the time of the irradiation. This is the "young adult" age for the rabbit.

For most of the experiments, x-rays were delivered with the following factors: constant potential, 1,200 kv.; filament current, 0.4 ma.; half-value layer, 10 mm. Cu; output, 45 r per minute; object-target distance, 70 cm., and field, 25 by 25 cm. A description of the x-ray generator used has been given by Trump and Van de Graaff.[15] For some of the experiments, the radiation factors were as follows: full wave rectified pulsating 200 kv. peak; filament current, 20 ma.; half-value layer, 0.9 mm. Cu; output, 46 r per minute; object-target distance, 50 cm., and field, 20 by 20 cm.

The adult rabbits were immobilized in a box and so placed that the right eye and the right side of the head were in the beam, while the left side of the head and the rest of the body were outside the beam. To determine the dose which was reaching the eye, as altered by attenuation and scattering in the rabbit's head, the thimble of a Victoreen dosimeter was placed in a rabbit's orbit from which the eye had been enucleated. The amount of x-radiation in the orbit was found by measurement to be 3 per cent greater than that measured in air; this was less than the average error (5 per cent) in Victoreen measurement.

The dose range was 250 to 3,000 r for the 1,200 kv. x-ray exposures and 1,000 to 2,000 r for the 200 kv. x-ray exposures. A dose of 3,000 r was chosen as the upper limit, since this corresponds to the heavier doses to which human beings might be exposed. For the age study, rabbits were used at age levels of 3, 4, 6 and 10 weeks; 6 months, and 1½ years and 3 years. For each dose and age level, observations were made on a minimum of four eyes. All animals were examined at five day intervals during the first 20 days and at 10 day intervals thereafter. Especially noted was the presence or absence of epilation, keratoconjunctivitis and changes in

13. Rugh, R.: Histological Effects on the Embryo Following X-Irradiation, J. Morphol. **85**:483, 1949. Mottram, J. C.: Early Changes in Nucleus of Cells of Tumours Following Exposure to β Radiation, Brit. J. Radiol. **32**:61, 1927.

14. In a separate study, not reported here, no difference was found for the susceptibility to cataract in a group of chinchilla and a group of New Zealand white rabbits.

15. Trump, J. G., and Van de Graaff, R. J.: A Compact Pressure-Insulated Electrostatic X-Ray Generator, Physical Rev. **55**:1160-1165 (June 15) 1939.

the lens. The lenticular alterations were followed ophthalmoscopically through pupils that had been dilated with 4 per cent atropine. While slit lamp biomicroscopy was used occasionally, it was found less satisfactory for following the course of events than was ophthalmoscopy.

The histological studies were carried out by means of the usual cross sections of lenses that had been embedded in pyroxylin and by flat preparations of the lens capsules. The latter were prepared in part according to the technique described by Verhoeff,[16] using Zenker's fixation method, and in part according to the following, simpler technique: The lens was removed through a crucial incision of the sclera centering about the optic canal. Together with a few drops of water, the lens was placed on a glass slide epithelial side up. The slide was then placed on the pedestal of a freezing microtome, and the lens was frozen from the under side up until the area of freezing reached just above the equator. At this point the lens was bisected with a razor blade, and the entire anterior half of the lens was placed, capsule side down, on another glass slide. If the edges of the capsule were gently patted down with a blunt instrument, the capsule could be made to adhere to the glass slide. Then, after a minute's drying, the whole cortical mass could be dislodged with a sliding and circular motion, leaving a clean and cortex-free capsule adherent to the slide. Flat preparations of the posterior capsule may be similarly prepared. The slides were then placed in a fixative and stained variously. The most satisfactory fixative was found to be Carnoy's, and the most satisfactory staining was with hematoxylin and fast green.

RESULTS

Epilation, keratoconjunctivitis and cataract were the outstanding abnormalities following irradiation of the ocular region. Xerosis was an occasional occurrence after the severest exposures.

Epilation.—This varied from a minimum of barely perceptible loss of hair on the lid margins to a maximum of complete loss of hair for several centimeters about the eye.

With the 1,200 kv. radiation and 10 week old rabbits the latent period for minimal epilation was an inverse function of the dose in the range of from 1,500 to 3,000 r (fig. 1). No gross epilation was noted with measured amounts of radiation less than 1,500 r. There was considerable individual variation, but no constant variation in susceptibility with age.

With 200 kv. radiation and 10 week old rabbits, epilation occurred sooner and with lower measured doses, but the latent period was also an inverse function of the dose. Epilation occurred with doses as low as 1,000 r, which was the least amount studied with the 200 kv. radiation.

Keratoconjunctivitis.—The minimal symptoms of keratoconjunctivitis consisted of mild redness of the eye with slight purulent discharge and abnormal "take" of fluorescein by the cornea. The severer reactions consisted of frank corneal ulceration, with eventual cicatrization of the cornea. Band keratopathy occurred frequently in eyes after the development of cataract.

With the 1,200 kv. radiation and 10 week old rabbits the latent period for the development of keratoconjunctivitis, as in the case of epilation, was an inverse function of the dose. With 3,000 r the lesions developed approximately two weeks after the irradiation and led to a variable amount of cicatrization. With 1,500 to 2,000 r, the latent period was of the order of one month, and the keratoconjunctivitis only rarely led to opacification of the cornea. With radiations of 1,000 r, keratoconjunctivitis occurred in only one of four rabbits, and this only after a

16. Verhoeff, F. H., and Bell, L.: Pathological Effects of Radiant Energy on the Eye, Proc. Am. Acad. Arts & Sc. **51**:629, 1916.

latent period of 100 days. No keratoconjunctivitis occurred with exposures of 500 r. Younger rabbits appeared to have keratoconjunctivitis earlier, but there was considerable individual variation.

With 200 kv. radiation and 10 week old rabbits the keratoconjunctivitis occurred sooner and was considerably more profound than with the 1.2 mev radiation. With 2,000 r the keratoconjunctivitis began in 10 to 15 days and resulted in sufficient opacification and ulceration of the cornea within 30 days to prevent visualization of the ocular media. With 1,500 r the latent period was approximately 20 days. With 1,000 r only one of the four rabbits had keratoconjunctivitis, and this to only a mild degree.

In the severer instances of keratoconjunctivitis xerosis was also present to a degree that was grossly apparent.

The effect of the radiation on the lacrimal glands is to be reported separately.

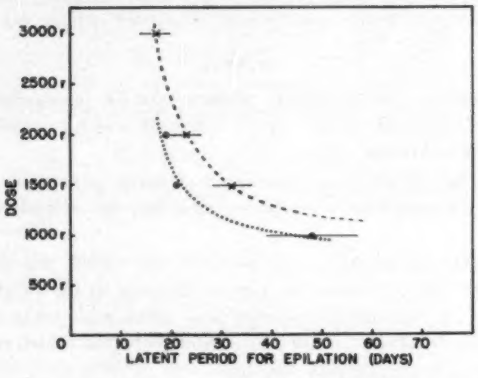

Fig. 1.—Relation of onset of epilation to dose of x-rays in 10 week old rabbits for 1,200 kv. (line of dashes and crosses) and 200 kv. (line of dots and circles). The mean variations for each point are represented by the horizontal lines.

Cataract.—(*a*) Morphological Features: Radiation cataract in the rabbit begins axially or peripherally. The axial changes began as vacuoles or granules in the posterior subcapsular region. With the lower doses, granular opacities generally began in the center of the suture line and progressed toward either end (fig. 2). With the higher doses, vacuoles developed first at either end of the horizontal suture (fig. 3 *A*) and progressed axialward, often forming a continuous line of vacuoles in the zone of the suture. Subsequently the vacuoles usually disappeared, leaving the central region clear. The granular opacities were also in the immediate subcapsular zone and came to be arranged in a roughly circular fashion, having a diameter corresponding to the horizontal suture (figs. 3 *B* and 4 *A*). Moreover, these opacities had a somewhat feathery appearance, with radiating lines corresponding to the distribution of lens fibers. This paracentral opacity, together with a variable amount of vacuoles, then progressed peripherad (fig. 4 *B*).

The peripheral changes similarly consisted of granular opacities and frequently vacuoles in the immediate subcapsular zone, with a feathery arrangement corresponding to the lens fibers. Forming initially a collaret at the extreme periphery,

these peripheral opacities progressed by extension axialward and ultimately merged with the paracentral opacities to form opacification of the entire posterior subcapsular region. The central area was the last portion to become opaque.

With radiation in excess of 1,000 r the central and peripheral changes appeared approximately at the same time, sometimes beginning with the one and sometimes

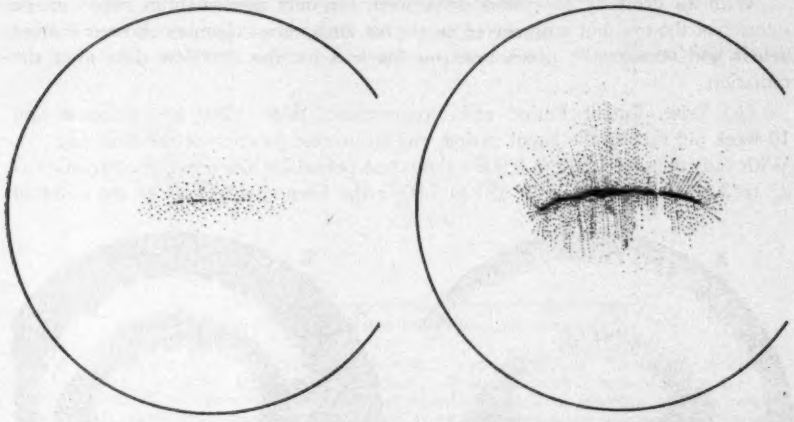

Fig. 2.—Diagrams representing successive stages of incipient cataracts with the lower doses of x-radiation (250 to 1,000 r), as seen with the ophthalmoscope.

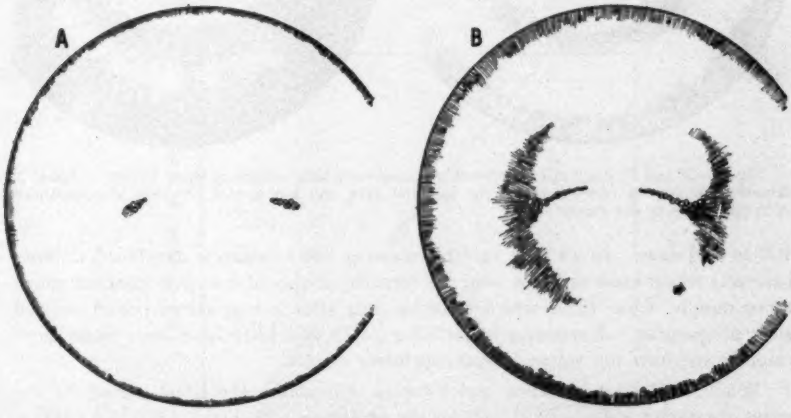

Fig. 3.—Diagrams representing the ophthalmoscopic appearance of cataracts found with doses of radiation greater than 1,000 r. (*A*) First, vacuoles occur at either end of the horizontal suture, and often granular opacities occur at the equator. (*B*) Both the central and the equatorial changes increase, and granular opacities occur in the paraxial region, having a characteristic feathery arrangement corresponding to the orientation of the lens fibers. Vacuoles then appear just anterior to the granular opacities.

with the other. The order of onset did not appear to be a function of age. With doses of less than 1,000 r there were initially central changes only.

When the opacities in the posterior subcapsular zone were well advanced, changes occurred in the anterior subcapsular region, predominantly in the pupillary zone, and were characterized by granular opacities and vacuoles. Soon thereafter the entire cortex, and ultimately the whole lens, became opaque to form a mature cataract.

With all ordinary exposures these were the only abnormalities noted in the interior of the eye, but with severe exposures the anterior chamber showed floating debris and occasionally precipitates on the lens for the first few days after the radiation.

(*b*) Dose, Latent Period and Progression: With 1,200 kv. radiation and 10 week old rabbits the latent period was an inverse function of the dose (fig. 5). With radiations of 1,500 to 3,000 r the latent period for the onset of cataracts was 25 to 30 days, whereas with 250 to 1,000 r the latent period was of the order of

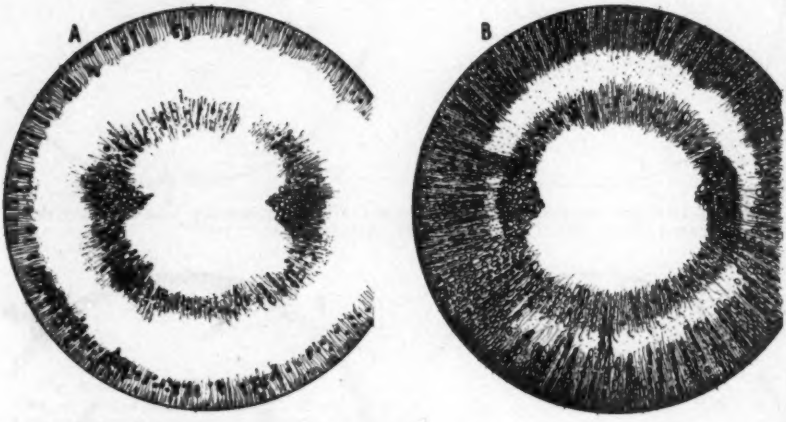

Fig. 4.—*A* and *B*, diagrams representing successively later stages of those shown in figure 3. Noteworthy are the completion of the paraxial ring and the almost complete disappearance of vacuoles along the suture line.

100 to 150 days. In all four rabbits receiving 250 r cataracts developed. Those cataracts which came on early after the irradiation also advanced to maturity much more rapidly, while those which came on only after a long latent period showed slow progression. Exposures to radiation of 75 and 150 r have been made more recently and have not yet permitted conclusive results.

With the 200 kv. radiation and 10 week old rabbits, the latent period for the onset of cataract was about 30 days for the exposures with 1,000, 1,500 and 2,000 r, but a precise correlation with dose was impossible on account of opacification of the cornea.

(*c*) Effect of Age: The latent period in the development of cataract was greatly affected by age. With exposure to 1,500 r or 1,200 kv. radiation, cataracts occurred after a progressively longer latent period (fig. 6). Thus, with 1,500 r cataracts appeared in 15 to 20 days in the 3 week old rabbit and only after 100 to 150 days in the 3 year old rabbits.

(*d*) Relation of Cataract to Epilation and Keratoconjunctivitis: With 10 week old rabbits and the higher doses of x-rays (2,000 to 3,000 r) epilation and keratoconjunctivitis preceded morphological changes in the lenses by as much as 2 weeks (figs. 1 and 5). With the intermediate dose of 1,500 r changes in the lens occurred

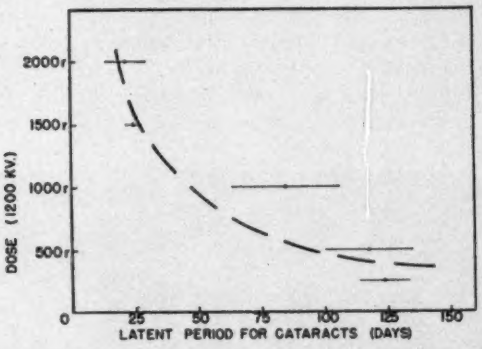

Fig. 5.—Relation of onset of cataract to dose in 10 week old rabbits. The average determination is indicated by a dot, and the mean variation, by the horizontal lines. Whether this is a linear, exponential or other function could not be determined from the data, but the curve is drawn as an asymptotic function, on the dual assumption that there would always be some latent period in the production of cataract (from the present process) even with infinitely large doses, and that there would be a threshold dose (possibly 250 r) below which cataracts would never develop. (Since the graph was made, two additional rabbits receiving 1,000 r exhibited cataracts on the seventy-fifth day.)

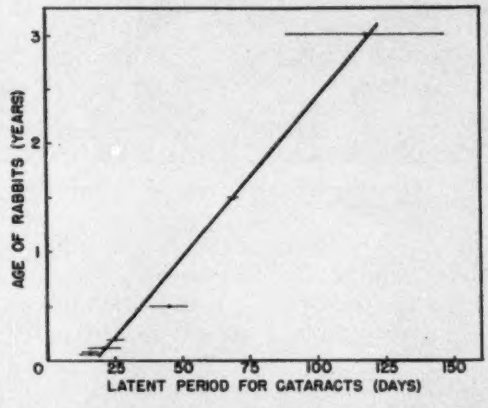

Fig. 6.—Relation of onset of cataract to age of rabbit. The mean variation is represented by horizontal lines. (Since the graph was made, 4 month old rabbits were found to have a latent period of 36 days.)

at approximately the same time as did epilation and keratoconjunctivitis. With smaller doses (500 to 1,000 r) epilation and keratoconjunctivitis either did not occur at all or else followed the changes in the lens. For the 200 kv. radiation the

epilation and keratoconjunctivitis preceded the changes in the lens with doses of 1,500 r or more. With doses of 1,000 r the changes in the lens preceded the epilation and keratoconjunctivitis.

(*e*) Histological Changes: The normal lens epithelium provides an ideal preparation for studying cytological changes resulting from irradiation (fig. 7). It consists of a single layer of remarkably uniform cells; mitoses are rarely seen in the normal epithelium.[8c] The only departure from uniformity is the somewhat smaller size of the cells toward the equator.[17] Occasionally one can see in flat preparations small round basophilic bodies, approximately one-half the size of the nuclei, to be found lying on the cortical side of the epithelium. These sometimes occur singly

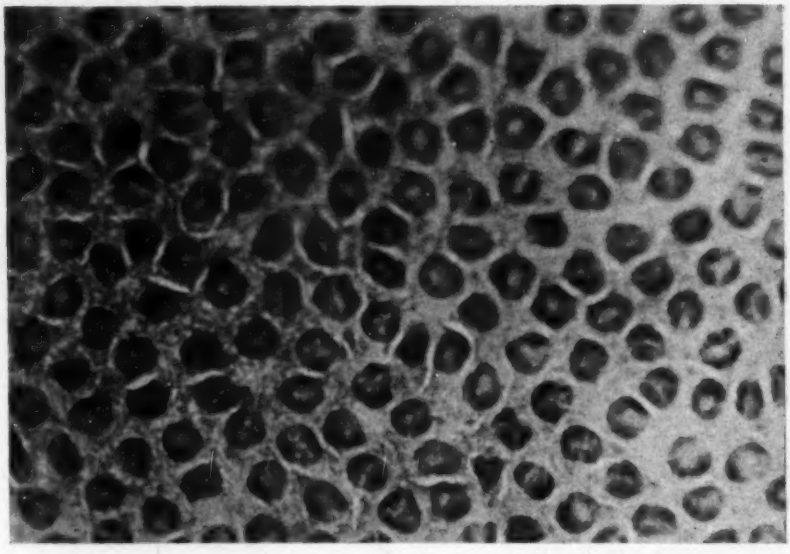

Fig. 7 (high power photomicrograph).—Normal flat preparation of lens epithelium of the rabbit showing characteristic uniformity of nuclei.

and sometimes in clusters; they are more frequent toward the equator. They are presumed to represent nuclei of cells which have extended into the lens cortex in the course of forming lens fibers, but it is to be noted that they are by no means found only in the equatorial region, where lens fibers are believed to be formed exclusively.

The cytological changes resulting from irradiation are both cytoplasmic and nuclear. Relatively common are cells having several times the normal complement of cytoplasm and separated from the rest of the epithelium by artefactual cracks (figs. 8 and 9). The cytoplasm of these cells is often vacuolated, but otherwise

17. When Zenker's fixation is used, the peripheral cells also show intercellular clefts, giving the appearance of "cracking"; this is not true with Carnoy's fixative.

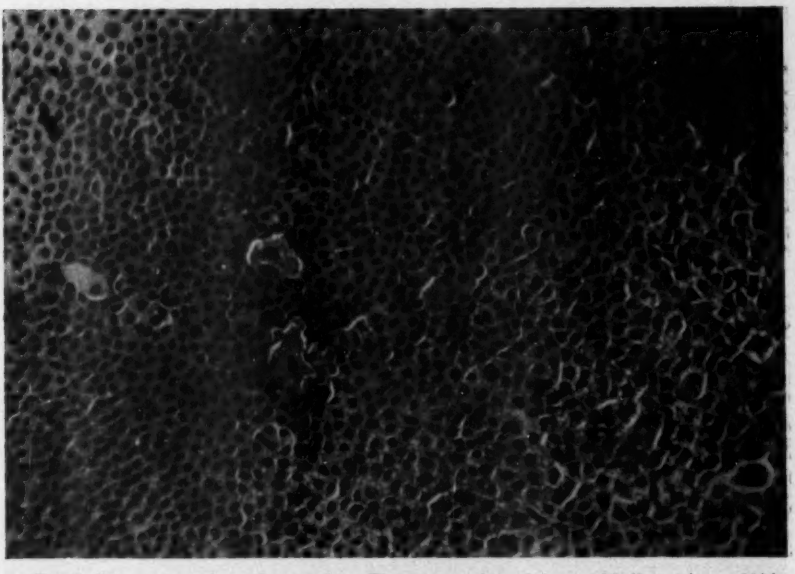

Fig. 8 (low power photomicrograph).—Flat preparation of lens epithelium of a rabbit's eye which had been exposed 100 days previously to 2,000 r and which showed at the time of enucleation an immature cataract. Characteristic is the occurrence of cells having abnormally large amounts of cytoplasm.

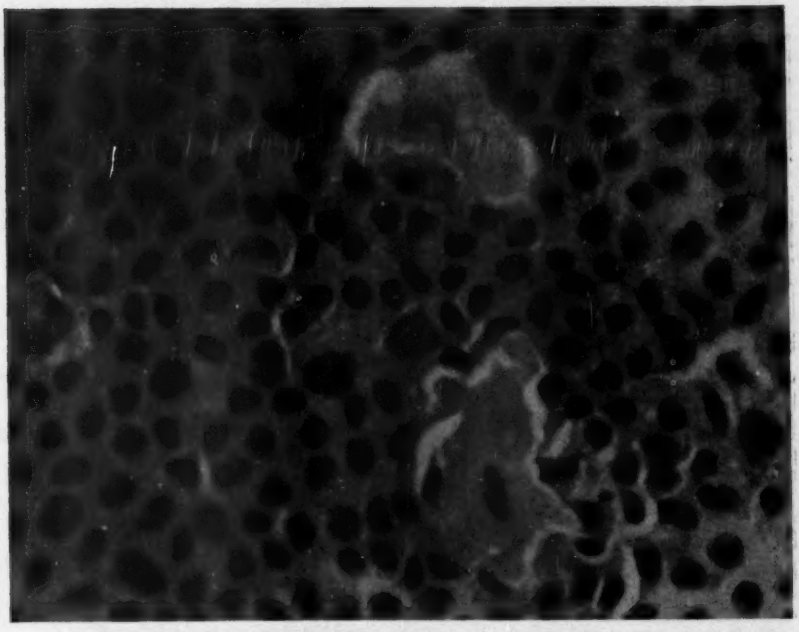

Fig. 9 (high power photomicrograph).—Selected field from the preparation shown in figure 8, illustrating the characteristic anisocytosis.

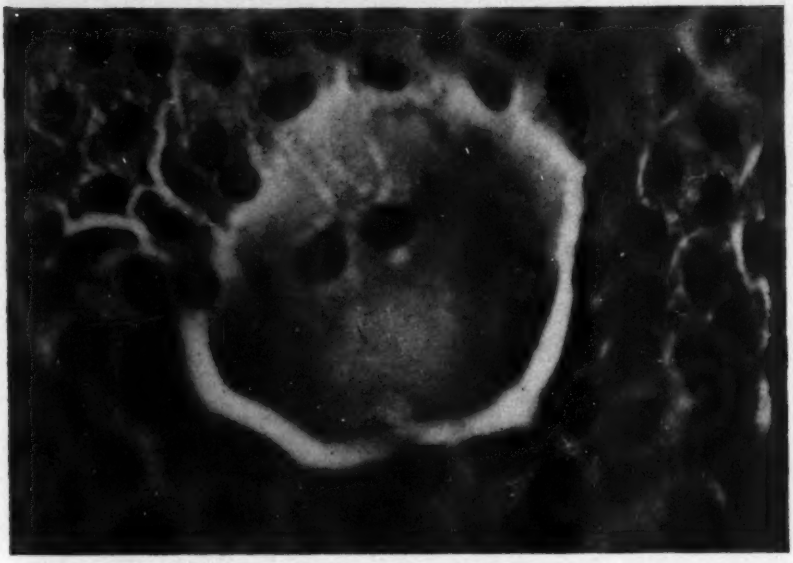

Fig. 10 (high power photomicrograph).—Selected field from the same preparation as that illustrated in figure 8, showing a giant cell with multiple nuclei.

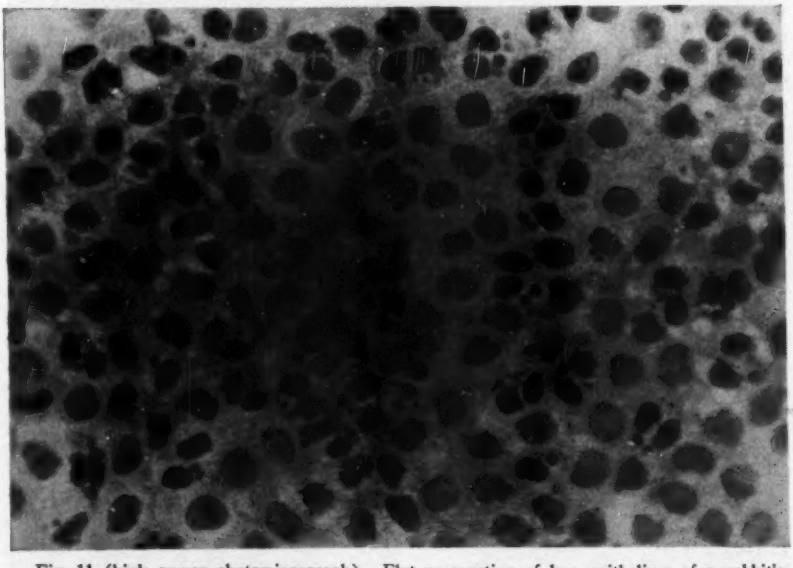

Fig. 11 (high power photomicrograph).—Flat preparation of lens epithelium of a rabbit's eye which had been exposed 150 days previously to a dose of 2,000 r and which showed incipient cataract at the time of enucleation. The specimen showed striking nuclear fragmentation.

has approximately normal-staining properties. These abnormally large cells may contain normal-appearing nuclei, enlarged nuclei or multiple nuclei (fig. 10). They usually occur as isolated phenomena, being surrounded by normal-appearing cells.

The nuclear changes are variable. Relatively common is the break-up of nuclear material into several spherical masses within the cell (fig. 11), a phenomenon which has long been described as an early stage of nuclear disintegration [18] often seen in malignant cells,[19] but which has been interpreted physiologically as a readjustment of the nuclear surface area in consequence of enlargement of the cell as a whole.[20] An advanced stage of this process is the occurrence of multiple hyperchromatic bodies in a cell without any recognizable nucleus (karyorrhexis). No

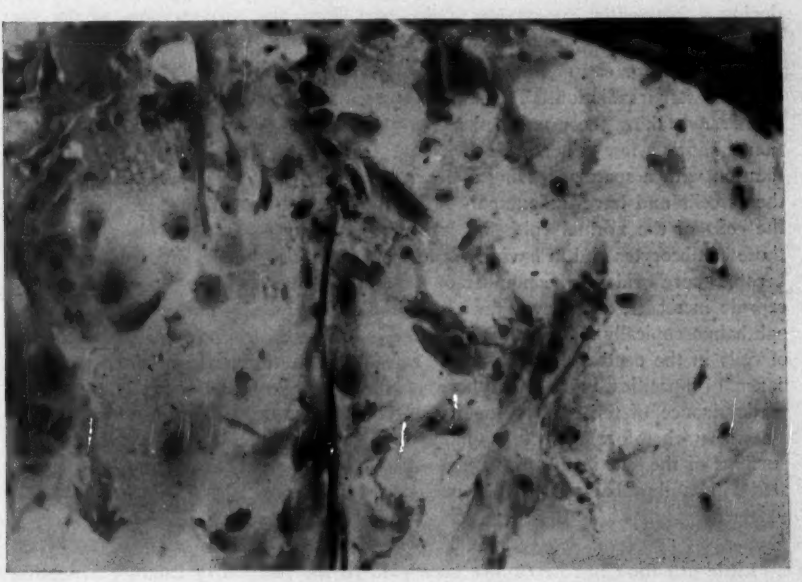

Fig. 12 (high power photomicrograph).—Flat preparation of posterior capsule from the same lens as that pictured in figures 8, 9 and 10. Noteworthy are the aberrant cells affixed to the posterior capsule. (The dark lines represent capsular folds, which are present with preparations of the posterior capsules.)

genuine mitoses were seen, but often paired cells were to be found that had nuclei which were smaller and more basophilic than the other cells, suggesting that they had recently divided.

These changes in the lens epithelium were more marked the greater the dose and the longer the time after the onset of cataracts; but they could also be found

18. Macklin, C. C.: Binucleate Cells in Tissue Cultures, Contrib. Embryol. **4**:69 (13), 1916.

19. Howard, W. T., and Schultz, O. T.: Studies in the Biology of Tumor Cells, Monograph 2, Rockefeller Institute for Medical Research, 1911.

20. Ludford, R. J.: Pathological Aspects of Cytology, in Bourne, G., editor: Cytology and Cell Physiology, New York, Oxford University Press, 1942, pp. 226-259.

antedating any clinical evidence of cataract. Thus, of 3 rabbits aged 10 weeks exposed to 1,500 r with 1,200 kv. x-rays the rabbit which was killed on the twenty-first day after irradiation showed the characteristic fragmentation of nuclei, although there was no gross sign of cataract at the time of enucleation. The eye that had been enucleated on the fifteenth day after irradiation showed no abnormality of the lens epithelium. In the surviving animal cataracts developed sometime between the twenty-first and thirtieth day after irradiation.

These morphological changes in the lens epithelium appear to be characteristic of exposure to radiation and have previously been described in part by von Sallmann and Poppe. Such changes were not observed with senile cataracts in man. Here the epithelium becomes vacuolated, and much of it may disappear entirely, producing a moth-eaten appearance of the epithelium; but there is none of the anaplasia of cells and fragmentation of nuclei such as is seen after irradiation.

The posterior capsule, prepared in a similar manner, shows equally interesting changes after irradiation. The normal posterior capsule is a uniformly translucent membrane, taking the usual stains poorly. In the early stages of cataract formation it shows a few cells affixed to it (fig. 12). These may be rubbed off prior to fixation with a spatula, leaving a clear capsule beneath. The cells stain like epithelial cells and have undoubtedly migrated from the equator. They differ from the cells of the normal epithelial layer, however, in having processes similar to those of fibrocytes and in having various-sized nuclei. As the cataractous changes become more evident, the number of these cells which are found on the posterior capsule increases, and they form a syncytial sheet. Those cataracts which showed ophthalmoscopically a predominance of the central opacities showed a predominance of cells in the central portions of the capsule, while those which had a predominance of opacities in the periphery of the lens ophthalmoscopically showed a predominance of the cells in the equatorial regions of the capsule histologically. There can, therefore, be little doubt that the granular opacification of the posterior portions of the lens in the early stages of radiation cataract in the rabbit is associated with, and probably due to, the presence of these cells.

COMMENT

Little attention has heretofore been paid to the relation of cataract formation to epilation and to keratoconjunctivitis after irradiation; yet these are the only reliable indexes, from a practical, biologic point of view, of the amount of radiation to the head region and may, as in the cases of exposure to atomic bomb radiation, be the only guide to the amount of radiation reaching the head region. The present studies indicate, for the rabbit at least, that acute exposures of less than 1,500 r (1,200 kv.) may produce cataract with no appreciable epilation or keratoconjunctivitis, and that age does not affect the animal's susceptibility to epilation and keratoconjunctivitis to anything like the same degree as to cataract.

These conclusions are opposed to those referred to by Desjardins as representing the sum total of evidence then available. This author stated, "The lens of adult animals (12 weeks or older) is remarkably insensitive, even to doses of roentgen rays several times stronger than the doses used in treating human beings," and as evidence cited the fact that animals which received doses sufficient to cause not only severe ulcerative radiodermatitis of the lids but also keratitis bordering on

perforation did not have cataracts. Whether this discrepancy between Desjardin's conclusions and our own is to be attributed to too short an observation period in the former case or to softer x-rays that were employed is not evident from the information given. But from our findings it may be stated categorically that the lens is a relatively susceptible organ to radiation with energies used in therapy (200 to 1,000 kv.) and that the threshold for production of cataract is less than that for any other gross abnormality of the eye or periocular tissue.

The question of individual predisposition to cataract following irradiation is often raised in the case of human beings, but no sufficient series of exposures under controlled conditions has been reported to permit of an answer. In the case of rabbits, cataracts occurred and progressed with remarkable uniformity when animals of one age level were exposed to the same amount of radiation, indicating no great individual predisposition other than that attributable to age.

It is occasionally suggested that radiation merely precipitates a latent tendency to the development of senile cataracts. Three facts contradict this statement. First, the morphological characteristics of radiation cataract and of senile cataract in human beings are entirely different. Second, rabbits which show a susceptibility to radiation cataract comparable to that of man are not known to have senile cataract. Finally, the greater susceptibility of the young to the development of radiation cataract is the reverse of what one would expect if the radiation precipitated senile cataract.

The morphogenesis of radiation cataract is of considerable interest. The cytological changes in the epithelium, preceding the opacification of the lens, suggest a disturbance of cell differentiation and are compatible with the hypothesis that radiation disrupts normal cell division. The cells at the equator appear no longer to be able to form normal fibers; rather, they remain globular or ellipsoidal at the equator and form at best abortive processes. Then, apparently, they migrate or are pushed toward the posterior pole between the cortex and the capsule, where they form the characteristic opacity of early radiation cataract.

What relation these cells have to the later opacification of the subjacent cortex is conjectural; but it seems reasonable to assume that it is the degeneration of these cells, with liberation of their intracellular enzymes, that causes the lysis of the cortex.

The cytological changes in the capsules do not account for the occurrence of vacuoles along the suture line. Perhaps this phenomenon is the direct result of the irradiation on the lens substance, but it seems more reasonably attributable to an alteration in the permeability of the lens capsule or to altered osmotic relationships, with consequent imbibition of fluid into the lens. Whatever the mechanism is, the localization of the vacuoles along the suture may be due to the lowered tissue pressure in this region. This locus minoris resistantiae is evident in microdissection of the unirradiated lens, and the predominant occurrence of vacuoles along the suture line may be artificially demonstrated by immersing a freshly excised lens in water. The vacuolation then simulates that which occurs in the early stages of radiation cataract. That this is a hydration phenomenon is evident by the increase in weight of the lens under these conditions and by the fact that these vacuoles along the suture do not occur when the lens is immersed in isotonic saline solution instead of in water.

SUMMARY AND CONCLUSIONS

With x-rays of 200 and 1,200 kv. energy in doses of 250 to 3,000 r and rabbits of ages ranging from 3 weeks to 3 years, the following effects were noted:

Epilation occurred in 15 to 35 days with doses of 1,500 r or greater, coming on sooner and being more profound the larger the dose and the less the energy of the x-rays. The threshold dose for epilation was 1,500 r for the 1,000 kv. and 1,000 r for the 200 kv. level. Little variation in susceptibility was found with age.

The same generalizations held for keratoconjunctivitis.

Cataracts likewise occurred with a latent period that was an inverse function of the dose; but, in contrast to the phenomena of epilation and keratoconjunctivitis, the threshold dose for 10 week old rabbits was 250 r or less, and the latent period for the development of radiation cataracts was much less, the younger the animal. With doses of x-ray (1,200 kv.) of less than 1,000 r, cataracts were the only abnormality produced.

Radiation cataract in the rabbit began with (1) an aggregation of vacuoles along the posterior suture line, oftenest at either extremity; (2) granular opacities, either scattered about the suture line or arranged in ring fashion in the paracentral region; and (3) an equatorial collaret beneath the posterior capsule. With the lower doses, the cataract began as scattered granules about the suture, whereas with the higher doses the cataract began as vacuoles at the end of the suture line. These granular opacities were due to epithelial cells, which, instead of forming fibers at the equator, as they do normally, had migrated posteriorly.

Cytological changes in the lens epithelium appeared to be characteristic of irradiation and could be found before any clinical evidence of cataract. The cellular changes consisted in the spotty occurrence of cells having several times the normal complement of cytoplasm and by nuclear fragmentation varying from mere budding to frank karyorrhexis.

DISTANCE DISCRIMINATION

VIII. Influence of Rod Brightness and Background Illumination in Howard-Dolman Test

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AND
M. J. HIRSCH, Ph.D. ‡
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HIRSCH, Horowitz and Weymouth [1c] have demonstrated that the apparatus rod size (width) does not affect the threshold but does significantly influence the position of subjective equality in tests of distance discrimination. It is known, in addition, that the apparent size of an object varies with the brightness of the object, this effect being due to irradiation (Duke-Elder [2]). In the Howard-Dolman apparatus the rods are painted dull black and have a different and weaker source of illumination than the background. Because of this arrangement the rods are seen essentially as silhouettes. Should the contrast between the rods and the background be lessened by decreasing the illumination of the background or by increasing the reflectivity of the rods, the factor of apparent rod size due to irradiation might alter the results obtained in testing with the apparatus, particularly if the reflectivity or brightness of the two rods differed. The purpose of this investigation is to determine the significance of the influence, if present, of rod brightness and background illumination and of the interrelationship of the two on the position of subjective equality.

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‡ At present at the Los Angeles College of Optometry.

From the Department of Physiology, Stanford University School of Medicine.

This paper is the eighth in the "Distance Discrimination" series, the others of which are listed in footnote 1.

1. (*a*) Hirsch, M. J., and Weymouth, F. W.: Distance Discrimination: I. Theoretical Considerations, Arch. Ophth. **39**:210-223 (Feb.) 1948; (*b*) II. Effect on Threshold of Lateral Separation of the Test Objects, ibid. **39**:224-231 (Feb.) 1948. (*c*) Hirsch, M. J.; Horowitz, M. W., and Weymouth, F. W.: III. Effect of Rod Width on Threshold, ibid. **39**:325-332 (March) 1948. (*d*) Hirsch, M. J.; Horowitz, M. W.; Walker, E. L., and Weymouth, F. W.: IV. Effect of Aniseikonic Lenses on Distance Discrimination, ibid. **39**:333-338 (March) 1948. (*e*) Hirsch, M. J., and Weymouth, F. W.: V. Effect of Motion and Distance of Targets on Monocular and Binocular Distance Discrimination, J. Aviation Med. **18**:594-600, 1947. (*f*) VI. Relationship of Visual Acuity to Distance Discrimination, ibid. **19**:56-58, 1948. (*g*) Wilner, B. I.; Weymouth, F. W., and Hirsch, M. J.: VII. Influence of Initial Position of Rods in Howard-Dolman Test, Arch. Ophth. **44**:365-369 (Sept.) 1950.

2. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1946, vol. 1.

THE EXPERIMENT

Methods.—The Howard-Dolman apparatus and procedure have been described in a previous paper.[3] The apparatus was altered for this experiment to obtain extremes in the conditions of rod brightness and background illumination. Aluminum-painted rods and dull black rods, in various combinations, were substituted for the black rods of the regular apparatus. The illumination of the background was altered to obtain brightness greater than or less than that on the rods. The rods were illuminated by room light, which was set at an intensity of 4 foot candles. The background was illuminated by two 8 watt fluorescent tubes to obtain a brightness of 6.5 foot candles—an illumination 2.5 foot candles greater than that of the rods; to obtain a brightness of 2.5 foot candles less than that of the rods, room light was allowed to reach the background, illuminating it to an intensity of 1.5 foot candles. Eight different situations of rod brightness and background illumination were obtained. These sets of conditions are tabulated.

	Stationary Rod	Movable Rod	Background Brighter	Rod Brighter	Abbreviation
1	Black	Black	+	..	BB2
2	Black	Black	..	+	BBO
3	Aluminum	Aluminum	+	..	AA2
4	Aluminum	Aluminum	..	+	AAO
5	Black	Aluminum	+	..	BA2
6	Black	Aluminum	..	+	BAO
7	Aluminum	Black	+	..	AB2
8	Aluminum	Black	..	+	ABO

Eight binocular readings were made with each of the eight sets of conditions by eight subjects with the Howard-Dolman procedure. The groups of eight readings were taken in sections of four readings each, the order changing with each subject, so that any influence of the conditions of one section on the readings of the following section would not affect the over-all data of the eight subjects. The following eight initial position settings, arranged in this random order, were used: + 100, + 400, — 400, — 200, — 300, + 300, + 200 and — 100 mm.

Results.—The conventional system of determining the position of subjective equality (E_s) of a subject with the Howard-Dolman test consists of measuring the position of the movable rod in relation to the stationary rod. The right rod, in general, is the movable rod of the pair, and the distance which it is placed either before (—) or beyond (+) the stationery (left) rod to appear at the same distance is a partial measure of the E_s. Since the E_s must distinguish between the right and the left rod, measurements of the position of subjective equality should consider the relative positions of the two rods, irrespective of which is movable. Two systems of measurement, therefore, are possible: one in which the same rod serves both as the stationary rod and as the point of reference for measurements (as in the conventional system), and one in which the rod of a designated quality is used as the point of reference, irrespective of whether or not it is movable. If the quality (reflectivity, etc.) of the rods is the same, the second possibility may be ignored; if the quality of the rods differs, on the other hand, an analysis of the results must consider both the laterality and the quality of the rods, regardless of which rod is stationary. With this point in mind, the results presented in the table may be considered.

1. Case in Which the Two Rods Are Alike: AA or BB: With the conventional system, in which a setting of the movable right rod farther than its fellow is considered positive (+) and nearer as negative (—) the E_s is seen to be affected by

3. Weymouth, F. W., and Hirsch, M. J.: The Reliability of Certain Tests for Determining Distance Discrimination, Am. J. Psychol. **58**:379-390, 1945.

the background illumination. With both AA and BB the E_s is greater with the brighter background (E_sAA2 > E_sAAO; E_sBB2 > E_sBBO); that is, the difference between the fixed and the movable rod is increased by a brighter background. This effect is more pronounced with the more reflective AA rods.

The reason for this relation is not clear. The average position of AA and BB rods for the two background illuminations must, however, be considered in evaluating the results for the mixed rods. The mean for AA2 and BB2 is + 7.75 mm., and that for AAO and BBO is + 0.27 mm.

The E_s is apparently affected by the change in background illumination regardless of the reflectivities of the pairs of rods. The effect on the E_s of the changes in rod reflectivities regardless of background illumination may now be considered. The means for AA2 and BB2, + 9.12 and + 6.39 mm., respectively, do not differ significantly, nor do the means for AAO and BBO, — 0.58 and + 1.12 mm. A difference in pairs test performed on the individual readings of AA2 and BB2, and AAO and BBO, respectively, produced t values of 1.15 and 0.77, with probability

Means of Readings Made by Subjects Under Eight Conditions (E_s) by Conventional System of Measurement†*

Subject	BB2	AA2	BA2	AB2	BBO	AAO	BAO	ABO
1	— 0.25	— 9.75	— 12.00	— 11.62	— 12.88	— 14.88	+ 16.62	— 31.50
2	+ 6.62	+ 25.25	— 65.38	+ 8.00	— 12.00	+ 13.00	— 42.25	— 69.88
3	+ 21.00	+ 25.62	— 3.12	— 3.50	+ 8.75	— 14.00	+ 9.88	— 56.75
4	+ 14.00	+ 12.00	+ 20.50	+ 3.38	+ 17.75	+ 14.75	+ 59.50	— 29.25
5	+ 3.75	+ 4.00	+ 11.50	+ 5.25	+ 9.00	+ 0.38	+ 28.88	— 37.75
6	+ 1.75	— 3.25	+ 1.62	+ 3.75	+ 0.50	— 5.00	— 1.12	— 27.62
7	— 11.12	— 6.25	— 3.00	— 8.75	— 6.00	— 10.38	+ 0.25	— 25.50
8	+ 15.38	+ 25.38	+ 0.62	+ 19.38	+ 3.88	+ 11.50	— 9.75	+ 1.00
Mean of total	+ 6.39	+ 9.12	— 6.16	+ 1.99	+ 1.12	— 0.58	+ 7.75	— 34.60

* In this table, BB2 indicates black stationary and black movable rod with background brighter; BBO, black stationary and black movable rod with rod brighter; AA2, aluminum stationary rod and aluminum movable rod with background brighter; AAO, aluminum stationary rod and aluminum movable rod with rod brighter; BA2, black stationary rod and aluminum movable rod with background brighter; BAO, black stationary rod and aluminum movable rod with rod brighter; AB2, aluminum stationary rod and black movable rod with background brighter; and ABO, aluminum stationary rod and black movable rod with rod brighter.

† The negative sign indicates that the movable (right) rod was nearer the observer than the stationary (left, reference) rod; the positive sign, that it was farther. Measurements are in millimeters.

values of approximately 0.10 and 0.40, respectively (63 degrees of freedom). A null hypothesis of no significant difference between the mean of the differences and zero is supported in each case. One may conclude, therefore, that rod reflectivity does not affect the E_s when both rods have the same reflectivity, whatever that may be, regardless of the level of background illumination.

2. Case of Two Rods of Different Reflectivities: AB and BA: If the B rod is taken as a point of reference in considering the rods of different reflectivities, in the case of BA the reference rod is the same as the stationary one, and the measurements obtained in the conventional manner may be considered directly. The E_s of BA2 is — 6.16, and that of BAO is + 7.75 mm. But these values must be corrected, as stated above, for the effect of the two levels of background illumination on pairs of rods of the same reflectivity. Subtracting the correction values from those just given, we have

$$\text{BA2} = -6.16 - 7.75 = -13.91$$
$$\text{BAO} = +7.75 - 0.27 = +\ 7.48$$

Treating the values obtained for the other mixed sets in the same way, we have

$$AB2 = +\ 1.99 - 7.75 = -\ 5.76$$
$$ABO = -\ 34.66 - 0.27 = -\ 34.93$$

In the case of the last two values, however, it must be remembered that the errors have been measured with reference to the stationary A rod. For the present consideration, these values must be converted so that they express, as in the case of BA2 and BAO, the errors with reference to the B rod. The conversion consists of changing the signs of the values:

$$AB2\ (\text{corrected}) = +\ 5.76$$
$$ABO\ (\text{corrected}) = +\ 34.93$$

If, now, we consider the effect on these corrected values of shifting the background illumination from bright to dim with the rods of different reflectivities, we have, subtracting the bright position from the dim:

$$BAO - BA2 = +\ 7.48 - (-\ 13.91) = +\ 21.39$$
$$ABO - AB2 = +\ 34.93 - (+\ 5.76) = +\ 29.17$$

It will be seen that the shift from the bright to the dim background causes the A rod to be placed in each case a considerable, and approximately equal, distance farther than the B rod to appear at the same distance as its fellow. We must assume that this effect is the result of the difference in reflectivity between A and B, and we believe that the effect of this difference operates by changing the apparent size of the rods by irradiation.

Helmholtz states [4] that at the boundary between two areas differing in brightness, the brighter invades the dimmer by an amount proportional, except at high illuminations, to the difference in brightness. On this basis, we may expect that with the brighter background both rods will appear smaller, although the exact amount is not easily estimated. In the case of the dimmer background, rod B, being less bright, will appear smaller, whereas rod A, being brighter than the background, will increase in size. If on the whole rod A appears larger against the dimmer background, it would have to be placed farther to appear the same size as its fellow. On this basis our results seem consistent with the assumption that the apparent size of the rods as affected by irradiation is the determining factor.

CONCLUSIONS

Case 1 has shown that the E_s is greater when background illumination is high than when it is low, regardless of whether the pairs of rods have great or no reflectivity. Although the reason for this result is not clear, the fact that the level of background illumination can affect the E_s in cases of rod pairs of identical reflectivities must be kept in mind in administering the test. This case has also shown that the reflectivity of the rods does not affect the E_s with either high or low level background illumination when the pairs of rods have the same reflectivity.

Case 2 has shown that when pairs of rods of differing reflectivities are used the shift from a bright to a dim level of background illumination causes the brighter rod to be placed farther from the subject than the dull rod, regardless of which

4. Helmholtz, H.: Helmholtz's Treatise on Physiological Optics, edited by J. P. Southall, Ithaca, The Optical Society of America, 1924, vol. 2, pp. 188-189.

rod is movable. This effect on the placement of the brighter rod we believe to be due to its apparent larger size, an effect, in turn, due to irradiation.

On the basis of these results we may recommend that in administering binocular distance discrimination tests with the Howard-Dolman procedure the following points be observed: (1) The level of background illumination should be kept constant throughout the examination or series of examinations, and (2) the rods should have identical brightness, whatever that brightness may be.

SUMMARY

From examination of 512 binocular distance discrimination readings made by eight subjects with the Howard-Dolman apparatus altered to obtain extremes in rod brightness and levels of background illumination, the following points were demonstrated:

1. The level of background illumination may influence the position of subjective equality (E_s) regardless of the reflectivities or brightnesses of the pairs of rods when the reflectivities of the rod pairs are identical; this effect is greater with rods of high than with rods of low reflectivity.

2. The reflectivity of the rods does not affect the E_s with either high or low levels of background illumination when the reflectivities of the rod pairs are identical.

3. The shift from bright to dim levels of background illumination in the case of pairs of rods of differing reflectivities causes the brighter rod to be placed farther from the subject than the dull rod. This effect is thought to be due to a difference in apparent rod size, which, in turn, is due to the phenomenon of irradiation. This fact demonstrates an effect on the E_s of both the level of background illumination and the rod brightness when the pairs of rods have differing reflectivities.

These points must be kept in mind when administering the Howard-Dolman test if the results of the test are to be a valid measure of the cues of distance discrimination which the test examines.

INTRAOCULAR INFECTION WITH THE GAS-FORMING BACILLUS CLOSTRIDIUM WELCHII

Report of a Case

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A CASE of panophthalmitis due to the gas-forming organism Clostridium welchii (Clostridium perfringens) was reported in this country by Berry in 1932.[1] Since then four cases have been added to the American literature [2] and 23 to the foreign.[3] The report by Klüver and O'Brien [2b] gives an adequate review of the foreign literature up to 1936 and of the laboratory identification of the Cl. welchii bacillus.

REPORT OF CASE

A laborer aged 27 was admitted to the Cleveland Clinic Hospital on Nov. 24, 1950. The personal and medical histories were noncontributory.

Twenty-eight hours prior to admission the patient had been struck in the left eye by a small fragment from the inside cement framework of a cellar window on which he was chipping with a hammer and chisel. The window was opened only for coal deliveries. He was not conscious of discomfort until three hours later, when the left eye began to water, with consequent irritation. Six hours after the accident he saw an ophthalmologist in his city, who placed ointment in the eye and administered one intramuscular injection of crystalline procaine penicillin G (crysticillin®). During the night the eye became painful, and at the time the patient was observed, 28 hours after the accident, he was in extreme pain, had been vomiting and had not eaten for 12 hours.

His vision was reduced to light perception, but on removing a thick heavy yellowish exudate, which seemed to arise from a faint gray line about 3 mm. long near the center of the cornea, the patient was able to perceive hand movements. The entire cornea stained with fluorescein, and the dye moved quickly into the anterior chamber. The cornea was cloudy, and the entire circumference was occupied by a whitish ring, which had the appearance of an annular abscess. Slight edema of the upper lid and reddish discoloration were present. The conjunctiva was chemotic, and there were a few subconjunctival hemorrhages. A bubble of gas, which measured approxi-

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From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

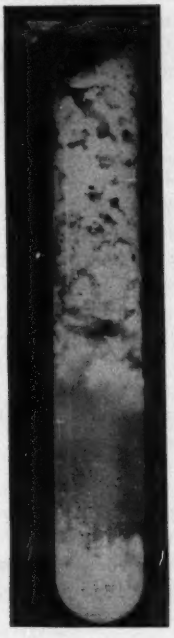
1. Berry, E. M.: Intraocular Foreign Body with Bacillus Welchii Infection, Am. J. Ophth. **15**:1022 (Nov.) 1932.

2. (*a*) Walker, S., Jr.: Bacillus Welchii Panophthalmitis, J. A. M. A. **102**:1561 (May 12) 1934. (*b*) Klüver, H. C., and O'Brien, C. S.: Panophthalmitis Due to Clostridium Welchii, Arch. Ophth. **15**:1088 (June) 1936. (*c*) Walker, S., Jr.: Prognosis of Bacillus Welchii Panophthalmitis, ibid. **19**:406 (March) 1938. (*d*) Capus, B.: Clostridium Welchii Panophthalmitis: Report of a Case, ibid. **36**:226 (Aug.) 1946.

3. Cross, A. G.: Gas-Gangrene of the Eye, Lancet **2**:515 (Nov. 1) 1941. Rieger, H.: Wound Infection of Eye with Irritants of Gas-Gangrene Group, Arch. Ophth. **17**:61, 1937. Canon, G.: Gas Bacillus Infection of Human Eye, Klin. Monatsbl. Augenh. **100**:394 (March) 1938.

mately 4 mm. in diameter, was seen in the anterior chamber. A roentgenogram of the orbit did not reveal any opaque foreign body. General physical examination and laboratory studies revealed nothing significant. The patient was given tetanus antitoxin U. S. P., 1,500 units, intramuscularly on admission and was started immediately on a regimen of 100,000 units of aqueous penicillin administered intramuscularly every three hours and instillation of aureomycin hydrochloride, aqueous solution, 2 drops every two hours, following gentle irrigation of the cul-de-sac. Morphine sulfate, 1/6 grain (10 mg.), was given immediately and every three hours, as necessary.

A culture of the thick exudate was taken after his admission. On the following day the yellow discharge continued through the perforation in the center of the cornea and was so profuse that the dressing had to be changed every two hours. Small brownish particles noted in the exudate were assumed to be disorganized uveal tissue. On the second day the patient was



Culture showing production of gas and whey after 24 hours in milk medium.

more comfortable and was able to take oral nourishment. The entire anterior chamber had filled with thick yellowish material, and the exudation through the corneal wound had lessened considerably. The lids and the conjunctiva remained swollen and red. Sixty hours after admission an evisceration was performed; at the time no gas bubbles were seen, although obviously the entire contents of the eye were destroyed and replaced by necrotic uveal material, fibrin and pus. The contents of the eye were gelatinous rather than fluid in appearance. Examination of this material failed to reveal any foreign body, and a culture was taken from the posterior part of the eye. Cultures of the wound were obtained several times after operation. The swelling of the lids decreased rapidly, and convalescence was uneventful. Fifty thousand units of polyvalent gas gangrene antitoxin was administered prophylactically after the operation.

Laboratory Studies.—Studies of exudates on admission and necrotic material taken from the posterior chamber of the eye at evisceration showed pure cultures of Cl. welchii. The figure

shows the violent evolution of gas which was produced in a milk medium and its characteristic separation into whey and coagulum. All cultures obtained postoperatively failed to yield gas bacilli.

One-tenth cubic centimeter of thin supernatant fluid from a 24 hour culture in the milk medium was injected intraperitoneally into a white mouse. The animal was killed with ether five hours after the inoculation, and several gram-positive nonmotile rods were demonstrated in the heart blood.

COMMENT

It is interesting to note that the course of this type of panophthalmitis, which usually results in extreme pain, high temperature, production of foul-smelling gas bubbles, blood-tinged turbulent liquid and necrotic uveal material, was interrupted in this case. After the institution of intensive systemic penicillin therapy, the gas bubble first observed in the anterior chamber was replaced by a yellowish, thick exudate, which gradually decreased in volume; on the day of operation there was little discharge issuing from the perforation in the center of the cornea. The patient's temperature was only slightly above normal during the period between admission and operation, while the agonizing pain had decreased greatly 12 hours after admission.

Penicillin in the treatment of gas bacillus infection of body wounds has proved to be the most valuable therapy available,[4] but experimental evidence in the use of penicillin and sulfonamides in controlled infections of the rabbit eye with Cl. welchii shows that when a lapse of more than three hours after inoculation occurs, local (including intraocular injection) and systemic therapy is of limited value.[5]

Examination of a patient and diagnosis within this three hour interval is, unfortunately, rare. Many of the histories show that the initial discomfort was slight and therefore often ignored from six to 12 hours. The virtual omnipresence of Cl. welchii has been demonstrated,[6] and it is likely that if routine cultures in cases of panophthalmitis were taken on thioglycollate broth more anaerobic infections of this type would be detected.

SUMMARY

This case is presented because of the relative rarity of reports in the United States of panophthalmitis due to Cl. welchii. It is the second recorded case in which antibiotics were used, and its course indicates that more intensive measures than those used are necessary in order to offer, even in the best of circumstances, a hopeful prognosis.

4. Gledhill, W. C.: Gas-Gangrene: Thirty-Three Cases, with One Death Treated at a Forward General Hospital in Italy, Lancet **2**:264 (Sept. 1) 1945. Hac, L. R.: Experimental Clostridium Welchii Infection: Penicillin Therapy, J. Infect. Dis. **74**:164 (March-April) 1944.

5. Hoskins, L. C.: Penicillin Therapy and Experimental Infections of Lens and Vitreous with Clostridium Welchii, Arch. Ophth. **38**:301 (Sept.) 1947. von Sallmann, L.: Penicillin and Sulfadiazine in Treatment of Experimental Intraocular Infections with Staphylococcus Aureus and Clostridium Welchii, ibid. **31**:54 (Jan.) 1944.

6. Kirz, E.: Gas Gangrene After Amputation Under Refrigeration Anesthesia: Warning, Brit. M. J. **2**:662 (Nov. 18) 1944. MacLennan, J. D.: Anaerobic Infections of War Wounds in Middle East, Lancet **2**:94 (July 24) 1943. Wan, F. E.: Gas Bacillus Infection: Review of Its Etiology, Symptomatology, and Treatment, China M. J. **44**:97 (Feb.) 1930. Altemeier, W. A., and Gibbs, E. W.: Bacterial Flora of Fresh Accidental Wounds, Surg., Gynec. & Obst. **78**:164 (Feb.) 1944.

CORTISONE THERAPY IN CASE OF RHEUMATOID NODULES OF THE EYE IN CHRONIC RHEUMATOID ARTHRITIS

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THE VALUE of cortisone in the treatment of various diseases of the eye has been reported by numerous investigators.[1] Reports from Merck & Company claim beneficial results in phlyctenular conjunctivitis, keratitis, iritis, iridocyclitis, uveitis and sympathetic ophthalmia.[2] Beneficial effects may result when the drug is administered intramuscularly, by instillation of a saline suspension or by subconjunctival injection; and it is expected that the oral route will prove efficacious. The first two modes of therapy were used in the present case.

The commonest ocular affections seen in conjunction with disease of joints (especially rheumatoid arthritis) are keratoconjunctivitis sicca (Sjögren's syndrome), episcleritis, primary uveal disease, scleritis and conjunctivitis.[3] Various authors have reported rheumatic granulomas of the sclera, external ocular muscles, orbital tissue and uveal tract.[4] Nodular formations of other causes are described.[5]

From the Research Service, First (Columbia) Division, the Department of Ophthalmology, Goldwater Memorial Hospital, Department of Hospitals, and the Department of Medicine, Columbia University College of Physicians and Surgeons.

1. Woods, A. C.: Clinical and Experimental Observations on the Use of ACTH and Cortisone in Ocular Inflammatory Disease, Am. J. Ophth. **33**:1325 (Sept.) 1950. Thorn, G. W.; Forsham, P. H.; Frawley, T. F.; Hill, S. R., Jr.; Roche, M.; Staehelin, D., and Wilson, D. L.: The Clinical Usefulness of ACTH and Cortisone, New England J. Med. **242**:783 (May 18) 1950.

2. Therapy with Cortisone—Inflammatory Eye Disease, Cortone, A Syllabus, Rahway, N. J., Merck & Co., Inc. 1950.

3. Henderson, J. W., and Hollenhorst, R. W.: Clinical Observations on the Use of Cortisone in Ophthalmological Diseases: Preliminary Reports, Proc. Staff Meet., Mayo Clin. **25**:459 (Aug. 2) 1950. Stenstam, T.: On the Occurrence of Keratoconjunctivitis Sicca in Cases of Rheumatoid Arthritis, Acta med. scandinav. **127**:130, 1947. Mills, A. J. O.: Rheumatoid Iritis, Am. J. Ophth. **31**:2 (Feb.) 1948.

4. Franceschetti, A.: Les affections oculaires d'origine rhumatismale, Ophthalmologica **111**:242 (April-May) 1946. Abelsdorff, G.: Skleritis rheumatica mit typisch rheumatischen Veränderungen (Aschoffsche Knötchen), Klin. Monatsbl. Augenh. **89**:836, 1932. Babel, J.: Contribution à l'étude histologique du rhumatisme oculare (À propos d'un cas de scléroténonite, Ophthalmologica **104**:243, 1942. Marchesani, O.: Über rheumatische Entzündungen des Auges, Klin. Monatsbl. Augenh. **106**:1 (Jan.) 1941.

5. Berens, C.: The Eye and Its Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1949.

Episcleral nodular tuberculosis may grossly resemble rheumatoid granulomas.[6] Except for the case described by Edström and Österlind[7] in 1948, we could find no others in the literature which resembled both clinically and histologically the case to be described. However, similar cases are not as rare as one might assume from the paucity of reported observations. Some few patients have recently been treated with either cortisone or pituitary adrenocorticotropic hormone (ACTH).[8]

REPORT OF A CASE

M. S., a single white woman aged 50, was admitted to the Goldwater Memorial Hospital Feb. 7, 1944, with a diagnosis of rheumatoid arthritis, which apparently began in 1942. It is interesting to note that, concomitant with the onset of swelling of the hands, fingers and right leg, the symptom most distressing to the patient was a protrusion of the right eye. Advised by two physicians to have the eye removed, she sought advice in the outpatient department of New York Hospital. She was treated with eye drops, and the condition disappeared in a short time, leaving no immediate residua. After attending the clinic for approximately six months, she was admitted to New York Hospital on Aug. 2, 1943 with the multiple complaints of loss of weight, edema of the eyelids, legs and hands, and an abdominal mass. Surgical intervention was recommended for the latter, and subtotal hysterectomy and bilateral salpingo-oophorectomy were performed. The diagnosis was fibromyomas of the uterus.

She entered Kings County Hospital in January 1944, where a hemorrhoidectomy was performed. Pertinent findings there included edema of the legs and ankles, an enlarged heart and enlargement of the liver. On multiple determinations the basal metabolic rates all ranged above + 16 per cent. Except for a hemoglobin content of 10 Gm. per 100 cc., the laboratory findings were normal. On becoming ambulatory after operation, she was transferred to Goldwater Memorial Hospital for treatment of rheumatoid arthritis. Diagnoses on discharge were hypertensive cardiovascular disease, chronic passive congestion of the liver, widespread arteriosclerosis and rheumatoid arthritis.

She had suffered very little pain until the time of her admission to this hospital, but in 1944 there occurred rapid progression of the disease to involve all the joints, including the cervical vertebrae. She received 2½ months of chrysotherapy and the usual palliatives for chronic arthritis. In the next two years there were noted enlargement of the thyroid gland, enlargement of the liver to 3 fingerbreadths below the costal margin, enlargement of the left auricle, as seen fluoroscopically and both systolic and diastolic aortic murmurs. The spleen was not palpable. In 1945 the patient suffered a fall and was confined to bed for weeks. Since that time she had never been completely ambulatory and at the time of admission had been confined to a wheel chair for at least four years. In 1948 she had an infection of the upper respiratory tract, accompanied with elevation of temperature for two months. In December 1949 the patient was in a rehabilitation ward with the diagnosis of chronic rheumatoid arthritis. At that time her sedimentation rate (Westergren technique) was 56 mm. in one hour; the hematocrit reading, 35 mm., the hemoglobin 70 per cent; the red blood cell count, 4,200,000, and the white blood cell count, 6,300. Her anemia did not respond to ferrous sulfate (feosol®) therapy. From March 16 to March 30, 1950, she received a course of pregnenelone (corpus luteum preparation), with little or no clinical response. The patient stated that the appearance of her joints had changed five or six times since admission. The past history was insignificant, and there was no history of allergy or of any symptoms resembling rheumatic fever.

The history of ocular involvement dated as far back as the original symptom complex, which included palpebral edema and protrusion of the right eye. Palpebral edema was again noted in 1943. In September 1945 the patient complained of decreasing vision and unilateral swelling of the right eye. She was given glasses and returned two months later with the complaint of excessive tear formation. At that time she had an irrigation of the lacrimal sacs. Examination in

6. Pollak, W.: Über isolierte Tuberkulose der Sklera unter dem Bilde eines Tumors, Klin. Monatsbl. Augenh. **88**:747 (June) 1932.

7. Edström, G., and Österlind, G.: A Case of Nodular Rheumatic Episcleritis, Acta ophth. **26**:1, 1948.

8. Ropes, M.: Personal communication to the authors. Heath, P.: Personal communication to the authors.

December 1947 revealed slight exophthalmos and periorbital edema. Vision was declared "good." Funduscopic examination showed normal disks and arteriosclerotic changes in the retinal vessels. In January 1948 she was again seen by members of the department of ophthalmology, this time complaining of a watery discharge from the eyelids. A consultant stated that she had moderate redundancy of the bulbar conjunctivas, more pronounced in the right eye. Pingueculae in the interpalpebral areas were considered as causing the existing irritation.

She was not seen again by the eye department until May 23, 1950, when a diagnosis of chronic catarrhal conjunctivitis was made. Vision at that time was 20/20 in the right eye and 20/25 in the left eye. Sulfacetimide ointment was applied sporadically, and use of aureomycin solution was ordered on June 6. Only slight improvement resulted. The patient was seen every two days, and on June 14 it was noted that she had bilateral episcleritis and pinpoint nodular formations in the interpalpebral areas nasally and temporally in both eyes. The corneas did not stain. It was believed then that the ocular pathologic process was rheumatoid in nature. Ethylmorphine hydrochloride (dionin), 0.5 per cent, was instilled in each eye, and she was placed on a regimen of instillations of 10 per cent sulfacetimide ointment; intramuscular injections of penicillin, 250,000 units three times a day, and application of hot compresses every two hours. Unfortunately, the administration of compresses and ointment did not follow the prescribed schedule. Atropine and scopolamine were both used, and on July 6 the conjunctival injection was markedly decreased and the patient subjectively improved. The cornea did not stain. Since the episcleritis still persisted to a minimal degree, the penicillin injections were discontinued and aureomycin hydrochloride, 500 mg. every six hours, was ordered on July 10. On July 17 a dramatic change took place.

What were originally pinpoint nodules suddenly, in the space of two days, developed into conspicuous nodular and plaquelike formations in the anterior scleral areas of both eyes. The nodules were raised and pale, with large dilated vessels seen between them. Except for a burning, gritty sensation, the patient experienced no pain throughout the course. From a picture of minimal ocular symptoms there was a change to the severest state. Color photographs were taken at this time. Topical cortisone therapy was instituted on July 20, the drug being instilled into each eye every hour during waking hours in a 1:4 dilution in sodium chloride solution. Atropine therapy was reinstituted and all other medication discontinued. Once again the patient's adherence to the medication schedule was poor. Despite this, minimal but definite improvement took place, and by August 7 the nodules had gradually disappeared inferiorly. On this date the available supply of cortisone was exhausted.

On August 16, nine days after cessation of local cortisone therapy, a severe exacerbation occurred. The nodules recurred inferiorly, and there was nodular formation to the same degree as on July 17. Slit lamp examination of the right eye revealed large mutton-fat keratic precipitates on the endothelial surface of the cornea inferiorly. The anterior chamber exhibited a 2 + flare, with fine cells noted in the aqueous. Posterior synechias were present. Though less marked, the same changes were present in the left eye. Tension (Schiøtz) was 25 mm. of mercury in each eye. The fundi appeared grossly normal. A diagnosis of iridocyclitis was made, with the most marked changes in the right eye. The patient was transferred to the Columbia University Research Division on August 23 for cortisone therapy.

Except for the severe ocular disease, the patient did not appear to be acutely ill. She was apprehensive and emotional but entirely cooperative. She was unable to turn herself in bed because of joint pain and muscular weakness. The effects of chronic rheumatoid arthritis and muscular atrophy were obvious. The temperature was 99.6 F.; the pulse rate 86 and the blood pressure 140/70. Four prominent, olive-sized subcutaneous nodules were present in the occipital area. Periorbital edema was present. The heart was not enlarged to percussion. A blowing, grade II systolic murmur was heard in all areas, being most pronounced at the sternal border in the left third interspace. The second sound in the second interspaces was more pronounced to the right of the sternum. The lungs were clear. The rib cage was deeply flared, and the liver was nontender and palpable from the right midclavicular line to the epigastrium. The spleen was not felt. Abdominal examination was noncontributory. The joints and extremities revealed classic evidence of rheumatoid arthritis. The red blood cell count was 3,900,000; the hemoglobin content, 11.0 Gm. per 100 cc.; the white blood cell count, 8,000; the hematocrit reading, 39 mm., and the erythrocyte sedimentation rate (Westergren), 87 mm. Fasting blood sugar measured 105 mg., blood urea nitrogen 19 mg., total serum cholesterol 162 mg. and cholesterol ester fraction 105 mg. per 100 cc.; thymol turbidity 3.6 units; cephalin flocculation test gave a 4 + reaction in 24

and 48 hours; the reaction to the Mazzini test was negative, and the serum sodium measured 136, the serum chloride 100, the serum potassium 4.5 and the carbon dioxide 29 milliequivalents per liter. The specific gravity of the urine was 1.010, and the urine showed no albumin, sugar or microscopic constituents. The total eosinophil count, with the phloxine-propylene glycol stain, was within normal limits.

Examination of the eyes revealed 3+ degree of corneal edema in each eye. Fine keratic precipitates were noted on the endothelium, with large mutton-fat deposits inferiorly in the right eye. The anterior chamber of each eye revealed floating keratic and 3+ flares. The pupil was 7 mm. in each eye. Synechias were seen in the right eye, but none were present in the left eye. Fine white and pigmented deposits were seen on the anterior lens capsules.

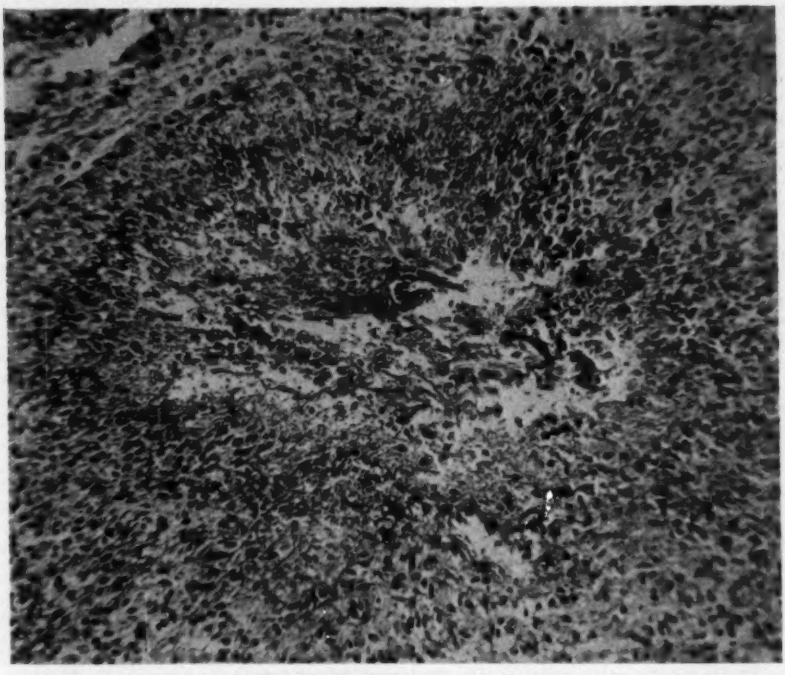

Fig. 1.—Section of sclera removed for biopsy before cortisone therapy, showing granulomatous lesion with necrotic center and palisading fibrocytes. Hematoxylin and eosin stain; × 216.

Tension (Schiøtz) was 48 mm. of mercury in the right eye and 35 mm. of mercury in the left eye, with a 10 Gm. weight.

A biopsy of one of the superior nodules in the left eye was performed. The nodule separated easily from the underlying and overlying tissues. The conjunctiva was found to be bound down and very friable. Two silk 4-0 sutures were used for approximation of the conjunctival margins, and a patch was placed on the left eye.

Grossly, the specimen was a small nodule about 4 mm. in diameter. Microscopic sections stained with hematoxylin and eosin revealed a granulomatous lesion with a necrotic basophilic center beneath an intact surface epithelium. About the necrotic material the young fibrocytes displayed a tendency to palisade. Interlacing strands of brilliantly acidophilic fibrinoid material streaked the connective tissue (fig. 1). Multinucleated foreign body giant cells were grouped about the necrotic area. Some of these cells had a foamy cytoplasm; others had phagocytosed fragments of fibrinoid material. Mononuclear foam cells were in close proximity to the giant

cells (fig. 2). Throughout the nodule was a pleomorphic cell infiltration, consisting of histiocytes, eosinophils, polymorphonuclear neutrophils and lymphocytes. Plasma cells were rare. The blood vessels were numerous but not remarkable. It was the opinion of the pathologist that this histologic picture was indistinguishable from that of a subcutaneous rheumatoid nodule.[9]

Since the condition was believed to have progressed beyond the point where local instillation of cortisone might be effective, the patient was given 300 mg. of cortisone acetate (cortone acetate®)[10] intramuscularly on August 24. She was closely observed every two hours during the first day, and no improvement was noted. On the contrary, on the following day there was 4 + corneal edema in both eyes. The right eye was capable of visualizing finger movements at no more than 3 inches (7.5 cm.), and the left eye, at 6 inches (15 cm.). In the left eye, extending across the iris and pupil from 11 to 7 o'clock, was an area of hemorrhage. Masses of fibrin

Fig. 2.—Multinucleated giant cells with fibrinoid material in the cytoplasm bordering an area of necrosis. Foam cells are present about and below the giant cells. Hematoxylin and eosin stain; × 302.

and red blood cells almost entirely occluded the pupil. Finger tension was increased in both eyes. A paracentesis was considered at this point but was not performed.

It was decided to continue treatment with administration of 200 mg. of cortisone acetate intramuscularly daily, and the dose was considered large enough to obviate use of multiple dose schedule. Arthritic pain improved on the second day, and she was nearly free from pain on the third day of therapy. The hemorrhage in the left eye was seen to be rapidly resolving, and on

9. Raven, R. W.; Weber, F. P., and Price, L. W.: The Necrobiotic Nodules of Rheumatoid Arthritis: A Case in Which Scalp, Abdominal Wall (Involving Striped Muscle), Larynx, Pericardium (Involving Myocardium), Pleurae (Involving Lungs), and Peritoneum Were Affected, Ann. Rheumat. Dis. **7**:63 (June) 1948.

10. Purchased with funds supplied by the United States Public Health Service.

August 28 it had completely cleared. The nodules were receding slightly, but corneal edema was still 4 +. The iridocyclitis was slightly less severe in the right eye, but the picture was worse in the left eye, with more numerous keratic precipitates and mutton-fat deposits. Without glycerin, finger counting was now done at 6 feet (1.8 M.) with the right eye and at 6 inches (15 cm.) with the left eye. Tension (Schiøtz) was 65 mm. of mercury in each eye.

On August 29, after five days and a total dose of 1,100 mg. of cortisone acetate, the patient claimed subjective improvement. Finger counting was at 1 foot (30 cm.) in the right eye, and vision in the left eye was 20/60. Improvement in the left eye was probably due partially to the subsidence of corneal edema, though finger tension was little changed. Slit lamp examination showed the condition of the right eye to be about the same as that previously described, and the deposits were becoming slightly pigmented. A 3 + flare was present. The left eye showed no corneal edema, a 1 + flare, no evidence of previous hemorrhage and diminishing keratic precipitates. The deposits remained on the lens capsule. The total eosinophil count on this day was 50 per cubic millimeter, and the erythrocyte sedimentation rate was 70 mm. in one hour.

On August 30 finger tension felt to be much reduced in both eyes. No change was seen in the vision of either eye. The biopsy sutures were removed, and another episcleral nodule removed *in toto* for pathologic examination. Healing of the previous incision was considered normal.

The second biopsy specimen was smaller and less satisfactory. It consisted mainly of epithelium and granulation tissue and a small part of what was probably a nodule. A small area of fibrinoid necrosis was present, about which were a few polymorphonuclear cells but few eosinophils. The cellular infiltration was predominantly lymphocytic and histiocytic. Plasma cells seemed more numerous than in the previous biopsy.

On September 1, the nodules were greatly decreased in size, and the dose of cortisone acetate was reduced to 100 mg. per day. Slit lamp examination revealed approximately 1 + corneal edema in the right eye, a decrease in keratic precipitates, a 2 + flare and persistence of the deposits on the lens capsule. The patient again claimed subjective improvement, and forms were now visible in the right eye. The sutures from the second biopsy were removed, and again the conjunctiva showed complete approximation and closure.

The nodules continued to decrease in size and number, and subjective improvement was evident. On September 6, after 12 days of cortisone therapy and a total dose of 2,100 mg., finger counting was at 6 feet in the right eye, and vision in the left eye was 20/50. Funduscopic study of the right eye revealed a disk normal in size and shape but with definite cupping. Slit lamp examination showed no corneal edema, a 1 + flare, no synechias, small and oval keratic precipitates and some folds in Descemet's membrane. The left eye showed no corneal edema, a plus-minus flare, practically no keratic precipitates and dustlike residual particles on the endothelium. On September 7 another biopsy was performed, the nodules now being barely visible.

The third biopsy specimen was similar to the first in that a small area of central necrosis persisted and about this the proliferating fibrocytes tended to palisade. The cellular infiltration, however, resembled that of the second biopsy specimen, with lymphocytes and histiocytes predominating. The striking clinical improvement was not reflected in any noteworthy change in the histologic picture (fig. 3).

Progressive improvement continued until, on September 11, vision in the right eye was 20/100 and only a few small keratic precipitates were seen. On September 13 vision was 20/100 in the right eye and 20/50 in the left eye. The nodules had then almost disappeared. Hyperemia of the bulbar conjunctivas and episcleras remained but was decreased. Finger tension was normal. Slit lamp examination showed the keratic precipitates rapidly resolving and disappearing. No synechias were seen. The left eye was quiet, and a plus-minus flare was present in the right eye. Vision in the right eye was entirely central, no peripheral fields remaining. On September 23, after one month of cortisone therapy, the dose was reduced to 50 mg. per day, with 100 mg. every other day. Vision was 20/50 in each eye. Of the four occipital nodules noted at the start of therapy, only two remained, and the other two were greatly diminished in size. The liver was still palpable. No change was noted in the blood pressure, and the heart sounds were the same. There was greatly increased motion of all parts, and the patient had no stiffness or tenderness. Contractures of the fingers showed definite improvement, and increased flexibility was obvious. The sedimentation rate fell from 94 to 42 mm. per hour (Westergren method). The reaction in the cephalin flocculation test at the end of three weeks had reverted from 4 + to negative. The thymol turbidity rose from 3.6 to 8.2 units. The total eosinophil count never

fell below 50 per cubic millimeter, obtained on the fifth day of therapy. At the end of a month the count was within normal range, the last being 238 per cubic millimeter.

Gain in weight was prominent during the first nine days of therapy. The patient lost 7 pounds (3.2 Kg.) after an injection of meralluride injection U. S. P. on the ninth day. Her weight did not reach the highest level again during the entire course. A facies characteristic of Cushing syndrome was prominent and persists at the time of writing. Her original pleasure at the saving of her eyesight and the well-being experienced on being free of arthritic symptoms reverted to a labile emotional status, with extreme irritability and depressive states.[11] We have noted this before in patients on continued cortisone therapy. Further, an episode of sudden weakness, diagnosed as hypopotassemia, was substantiated by finding a serum potassium level of 3.2 mEq. per liter, the initial value being 4.5 mEq.[12] An electrocardiogram showed low voltage T waves,

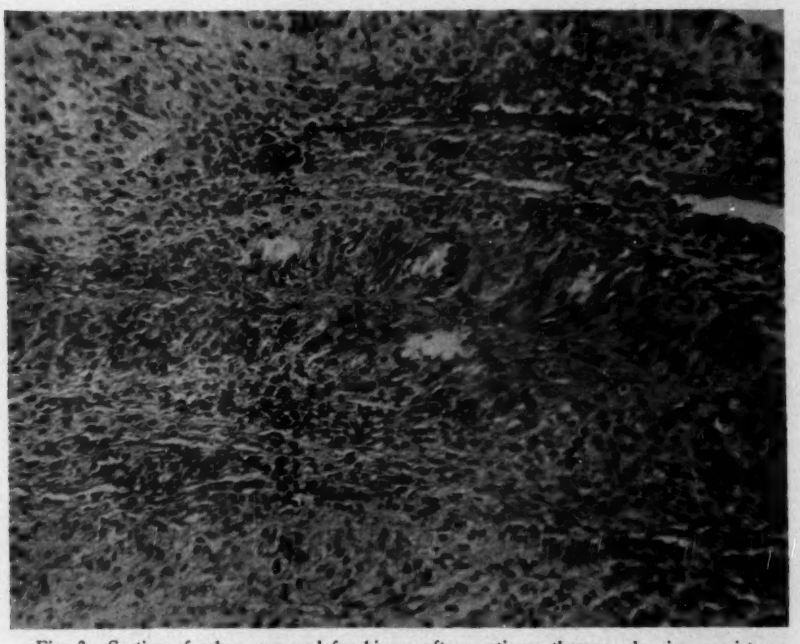

Fig. 3.—Section of sclera removed for biopsy after cortisone therapy, showing persistence of elongated granuloma. Palisading of fibrocytes is still present about a central area of fibrinoid necrosis. Hematoxylin and eosin stain; × 216.

but no change in the Q-T interval. Potassium chloride was given by mouth, with prompt relief of symptoms.

COMMENT

We do not consider the localization and restriction of the nodules to the episclera as constituting a distinct syndrome. It may well be that what we have seen is only the early stage of rheumatoid nodular growth in the eye, and that if the condition

11. Hoefer, P. F. A., and Glaser, G. H.: Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy: Electroencephalographic and Neuropsychiatric Changes in 15 Patients, J. A. M. A. **143**:620 (June 17) 1950.

12. Sprague, R. G.; Power, M. H.; Mason, H. L.; Albert, A.; Mathieson, D. R.; Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Observations on the Physiologic Effects of Cortisone and ACTH in Man, Arch. Int. Med. **85**:199 (Feb.) 1950.

had progressed we might have seen nodular involvement of the sclera and other tissues. There is no reason to believe that the process varied in its etiology or course from rheumatoid nodular syndromes with granulomas in other areas.

The regression of the nodules to the point where they were no longer grossly visible, yet with little or no change in the histologic picture, makes one wonder whether such minute nodules are not present in many cases of rheumatoid arthritis and never become an obvious sign of the disease. The histologic structure of the episcleral nodules is indistinguishable from that of subcutaneous nodules. Other investigators, studying the effects of ACTH and cortisone on the subcutaneous rheumatoid nodules, have not noted any notable histologic change under the influence of these compounds.[13]

The disappearance of the episcleral nodules may be related only to the improvement in the systemic disease. These nodules have an inherent "fugitive" tendency, waxing and waning with the underlying disease. The resolution of the intraocular inflammatory disease may be more directly attributed to cortisone. The response of inflammatory ocular disease to cortisone applied topically again raises the question as to the site of beneficial action of the drug. Numerous observations have pointed to its action at the tissue level.

We were interested in the healing process of the biopsy incisions.[14] The present view is that the effect of hyperadrenalism on wound healing is at the prefibroblastic level.[15] The defect in the process seems to be a delay in the formation of granulation tissue. Fibroblasts and proliferating blood vessels are retarded, and ground substance is scanty. The proliferation of epithelial structure is seemingly not affected.[16] The conjunctiva being predominantly epithelial in origin and the wounds created so shallow, we expected adequate healing to occur. The intervals of seven, two and four days for suture removal were due to chance, but ideal for our observations.

SUMMARY

In a white woman aged 50 with a history of rheumatoid arthritis for eight years there developed rheumatoid nodules of the episcleras. Local cortisone therapy caused initial amelioration of the ocular disease, but on cessation of administration of the drug a severe exacerbation of the nodules occurred, as well as iridocyclitis and glaucoma. Intramuscular administration of cortisone brought about disappearance of the nodular formations and subsidence of the intraocular processes.

Arthritic symptoms and signs responded favorably. The patient exhibited changes in psyche in the form of irritability and depression and showed symptoms of hypopotassemia.

13. Sokoloff, L.: Personal communication to the authors.

14. Ragan, C.; Howes, E. L.; Plotz, C. M.; Meyer, K.; Blunt, J. W., and Lattes, R.: The Effect of ACTH and Cortisone on Connective Tissue, Bull. New York Acad. Med. **26**:251 (April) 1950.

15. Spain, D. M.; Molomut, N., and Haber, A.: Biological Studies on Cortisone in Mice, Science **112**:335 (Sept. 22) 1950.

16. Creditor, M. C.; Bevans, M.; Mundy, W. L., and Ragan, C.: Effect of ACTH on Wound Healing in Humans, Proc. Soc. Exper. Biol. & Med. **74**:245, 1950.

THE FREE COMPOSITE LID GRAFT

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BIRMINGHAM, ALA.

ALL METHODS of replacing sectors of complete lid thickness loss have been based either on the principle of advancing flaps constructed in the lid itself or on the principle of transposing required lid tissue from nearby areas or across the palpebral fissure from the opposing lid.

The best method of repairing small colobomas of the lid (up to about 4 mm.) is by constructing a pedicle flap of the lateral lid fragment and the skin and subcutaneous tissue of the zygomatic and temporal region and advancing it to the medial lid fragment, the edges being united by the halving repair. Its only disadvantage is that the end of the lid margin remains bare of lashes, a more objectionable feature in the upper than in the lower lid.

If the loss is more than 4 to 5 mm., this method is usually contraindicated because the necessary medial advancement of the anterior lamina of the lateral flap will leave a large portion of the new margin bare of cilia and the absence of conjunctiva would be difficult to manage. Moreover, if the posterior lamina is freed from the lateral canthal ligament, the resulting canthotomy is likely to cause loss of the normal canthal angle, which is a considerable deformity in itself.

For the utilization of tissue from nearby areas, a variety of combined flaps can be used, such as the Fricke [1] or Imre flap or the double pedicle flaps of Sheehan.[2] These procedures require several stages, and it is usually necessary to allow subtotal intermarginal lid adhesions to remain in place for several months.

The best method of transposing lid tissue from the opposing lid is Hughes's reconstructive procedure, which utilizes the marginal half of the tarsus for the posterior lamina of the defective lid and employs a free skin graft or pedicle flap for the anterior lamina. His method has superseded and rendered obsolete other methods, such as Wicherkiewicz' and Esser's. An excellent functional and cosmetic repair can be achieved with it, and if the anterior lamina is to be reconstructed with a free graft of skin from below the eyebrow, cilia for the reconstructed lid can be obtained by including a few rows of the eyebrow hairs. One disadvantage of this procedure is that the lids must remain together for three or four months, vision being obstructed for this time, but a greater disadvantage is the difficulty of using this method for an upper lid. When Hughes's procedure is used for the lower lid, only three surgical procedures are needed; but when it is "reversed" and used for

From the Medical College of Alabama.

1. Fricke, J. C. G.: Die Bildung neuer Augenlieder (Blepharoplastik) nach Zerstörungen und dadurch hervorgebrachten Auswärtswendungen derselben, Hamburg, Perthes u. Besser, 1829.

2. Sheehan, J. E.: Plastic Surgery of the Orbit, New York, The Macmillan Company, 1927.

the upper lid, as many as seven operations may be necessitated, and several of these are difficult technically. Also, the series will require at least six months, and perhaps more, for completion.

Though these methods are of obvious value in most lid replacement problems, none of them is entirely adequate for large central colobomas of the upper lid. It is generally conceded that it is more difficult to reconstruct the upper than the lower lid because the requirements are greater. Anatomically, the tarsus of the upper lid is 10 mm. high, and half of it can easily be used to reconstruct the posterior lamina for the lower lid; but the tarsus of the lower lid is only 5 mm. high, and if it is divided between donor and recipient lids, neither is very strong and either may become distorted.[2a] Physiologically, if the levator is injured, ptosis will result; if the upper lid is too short, an exophthalmic appearance results. The upper lid must move frequently in blinking and with various directions of the gaze; the lower lid may remain rigid without much disturbance.

THE COMPOSITE LID GRAFT

To avoid the necessity of successive operations over a period of months, during most of which time the lids are necessarily joined together, a plan was conceived of shortening by half the horizontal extent of the defect and then attaching a free graft of the full thickness of the other upper lid—skin, subcutaneous tissue, orbicularis muscle, tarsus and conjunctiva.

Free grafting of either the skin or the posterior lid lamina has long been a standard procedure, but the grafting of the full lid thickness in a composite lid graft has not been reported, so far as I know. Brown and Cannon [3] have used composite free grafts of skin and cartilage from the ear for the repair of coloboma of the nose, and in 1948 Armstrong and Garcia [4] successfully used skin-cartilage-skin sections from the edge of the crus helicis of the ear in replacing marginal lid defects. These authors indicated the necessity of a secondary stage for removal of the skin on the inner aspect and its replacement with mucosa, if the eye was a seeing eye. The method now suggested has the advantage of being a one stage procedure, and it does not require that the lids be sutured together.

REPORT OF A CASE

The patient for whom this method has been used was 37 years old. A small wart of the lid had been treated by electrodesiccation, and it seemed to improve. However, after two months it began to grow, and during the two years that elapsed it became much larger. Clinically, it appeared to be a squamous cell carcinoma and involved the full thickness of the lid (fig. 1 *A* and *B*).

At operation, the tumor was removed with adequate margins of about 3 mm. of normal tissue on each side of the lesion. The lid measured 21 mm. from canthus to canthus; the operative coloboma, 11 mm. horizontally and 11 mm. vertically. This was slightly more than half the horizontal extent of the upper lid.

Later, microscopic study confirmed the diagnosis made from the clinical appearance.

Primary union was not to be considered because of the great degree of separation. Repair by either of the two methods outlined would encounter the difficulties discussed during operation or the many disadvantages as the stages proceeded.

2a. Callahan, A.: Surgery of the Eye: Injuries, Springfield, Ill., Charles C Thomas, Publisher, 1950.

3. Brown, J. B., and Cannon, B. S.: Composite Free Grafts of Skin and Cartilage from Ear, Surg., Gynec. & Obst. **82**:253-255, 1946.

4. Armstrong, C. J., and Garcia, F. A.: The Use of a Composite Graft in Reconstructive Surgery of the Lower Eyelid, Plast. & Reconstruct. Surg. **3**:79-83, 1948.

The first desiderium was to reduce the coloboma to half its horizontal dimension, utilizing the normal elasticity of the lid. At the coloboma margins the lids were separated into anterior and posterior laminas, and this division was extended above the coloboma to reach the upper tarsal margin (fig. 2, upper). Then, above the center of the coloboma a sector through the remaining tarsus was removed. This sector extended completely through the upper border of the tarsus and was 5 mm. wide (fig. 2, middle). The free edges of this second, and smaller, coloboma were joined with a mattress suture and several interrupted sutures (absorbable surgical suture U. S. P. 4-0) without difficulty, reducing the horizontal loss of the posterior lamina at the margin to about 6 mm. (fig. 2, lower). Though the anterior lamina had been separated at

Fig. 1.—*A*, squamous cell carcinoma involving the full thickness of the upper lid. This lesion developed in two years after electrodesiccation of a verruca vulgaris on the margin of the eyelid. *B*, appearance with lid closed.

the margins from the posterior lamina, the advancement of the sections of the posterior lamina toward each other brought the sections of the anterior lamina closer together. The coloboma then measured 11 mm. vertically, about 9 to 10 mm. horizontally in the anterior lamina and about 6 mm. horizontally in the posterior lamina.

From the right upper lid a section of the complete lid thickness was removed which measured 11 mm. vertically and 8 mm. horizontally (fig. 3, left). In making the incisions for the removal, the anterior and posterior laminas were offset about 2 mm. to permit the union in a halving method not only of the recipient lid, but also of the donor lid. To fit in the coloboma of the left upper lid, a lateral strip 2 mm. wide of the tarsus was discarded (fig. 3, left, inset). The graft

Fig. 2.—(Upper) The sector of full thickness of lid which has been removed measures 11 mm. vertically by 11 mm. horizontally. The distance from the medial to the lateral canthus along the upper lid is 21 mm. The anterior and posterior laminas are being separated along the margins of the coloboma to the dotted line.

(Middle) An additional sector of tarsus 5 mm. wide, and extending through the upper edge, is being removed.

(Lower) The edges of the smaller surgical coloboma have been brought together with absorbable surgical sutures U. S. P., and the horizontal extent of the larger coloboma is thereby shortened by half.

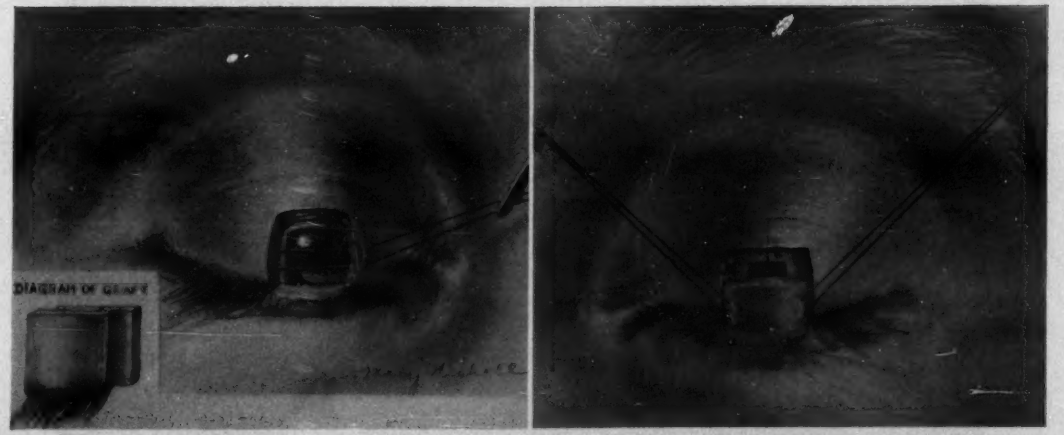

Fig. 3.—(Left) The composite sector of the right upper lid has been removed, and the halved edges of the resulting defect are being united with a Wheeler mattress suture. The inset shows the free composite graft, the dotted line indicating the tarsal edge which is to be discarded.

(Right) The composite lid graft is being fitted into the coloboma of the left upper lid.

Fig. 4.—(*A*) Appearance of the donor (right) lid four months later shows that no deformity has occurred. (*B*) The appearance four months after operation shows the viability of the composite lid graft. At no time were all cilia lost from the graft. (*C*) The lid closes easily, without excessive tension.

was then attached as rapidly as possible with interrupted sutures (silk [nonabsorbable surgical sutures U. S. P.] 6-0) to the coloboma (fig. 3, right). As this was performed, the composite lid graft became grayish.

Control of the horizontal tension in the donor lid was established with one mattress suture placed through the tarsus medially and the anterior lamina laterally, and reunion of the lid edges was performed with interrupted sutures (fig. 3, left). A moderately tight bandage was applied to both the donor and the recipient lid.

Examination a week later revealed the composite graft to be viable, and the donor lid showed only moderate reaction to the removal of the lid sector. The loose sutures were taken out, and on the tenth postoperative day all the sutures were removed.

Four months after operation the appearance of both the donor and the recipient lid was satisfactory (figs. 4 *A*, *B* and *C*).

SUMMARY

An original method which is applicable to repair of a large central coloboma of the upper lid is presented; it consists of reducing by half the horizontal dimension of the coloboma, into which is free-grafted a sector of the entire thickness of the other upper lid.

STUDIES IN EXPERIMENTAL OCULAR TUBERCULOSIS

XV. Effect of Paraaminosalicylic Acid and of Streptomycin plus Paraaminosalicylic Acid in Normal Rabbits

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SINCE the first reports by Lehmann [1] in 1946 on the use of paraaminosalicylic acid in tuberculosis, there have been an increasing number of reports on its value in experimental and human tuberculosis, both alone and in combination with streptomycin. The subject has recently been reviewed.[2] There have been a number of recent reports on the use of paraaminosalicylic acid in experimental ocular tuberculosis, as well as in cases diagnosed as ocular tuberculosis in humans.[3]

The following studies were undertaken to determine the effect of paraaminosalicylic acid, both alone and in combination with streptomycin, on experimental ocular tuberculosis in the normal rabbit. At the same time, these effects were compared with the effect of streptomycin and thiazolsulfone (promizole®; 4, 2′-diaminophenyl-5′-thiazolylsulfone) on experimental ocular tuberculosis in the normal rabbit.

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1. Lehmann, J.: Para-Aminosalicylic Acid in the Treatment of Tuberculosis: Preliminary Communication, Lancet **1**:15, 1946; Chemotherapy of Tuberculosis: The Bacteriostatic Action of Para-Aminosalicylic Acid and Closely Related Compounds upon the Tubercle Bacillus, Together with Animal Experiments and Clinical Trials with Para-Aminosalicylic Acid, Svenska läk.-tidning **43**:2029, 1946.

2. Bogen, E.; Loomis, R. N., and Hill, D. W.: Para-Aminosalicylic Acid Treatment of Tuberculosis, Am. Rev. Tuberc. **61**:226, 1950. Tucker, W. B.; Fellows, H. H.; Gale, J. W.; Jenkins, D. E.; Kirby, W. M. M.; Lincoln, E. M.; Schwartz, W. S.; Skavlem, J. H., and Trimble, H. G.: Current Status of Drug Therapy in Tuberculosis, ibid. **61**:436, 1950.

3. Lepri, G., and Fornaro, L.: Para-Aminosalicylic Acid in Experimental Ocular Tuberculosis, Arch. ottal. **53**:8, 1949; The Combination of Streptomycin and Para-Aminosalicylic Acid in Experimental Ocular Tuberculosis, ibid. **53**:129, 1949. Witmer, R., and Ragaz, L.: Pharmacologic Basis and First Results of Treatment of Ocular Tuberculosis with Para-Aminosalicylic Acid, Schweiz. med. Wchnschr. **79**:452, 1949. Lepri, G., and Capalbi, S.: Studies on the Chemotherapy of Experimental Ocular Tuberculosis, Arch. ottal. **53**:289, 1949. Gundersen, T., and Bietti, G. B.: Experimental and Clinical Investigations on Para-Amino-Salicylic Acid (PAS)—Alone or in Association with Streptomycin—in Ocular Tuberculosis, Tr. Am. Ophth. Soc. **47**:276, 1949. Bietti, G. B.: Use of Paraaminosalicylic Acid Alone or in Association with Streptomycin in Ocular Tuberculosis: Experimental and Clinical Observations, Arch. Ophth. **43**:431 (March) 1950. Rees, R. J. W., and Robson, J. M.: Experimental Tuberculous Infections of the Cornea of the Mouse: A Screening Test for Anti-Tuberculous Substance, Brit. J. Pharmacol. **5**:77, 1950.

EXPERIMENTAL STUDIES

Sixty-four healthy, normal adult rabbits, of mixed sex, averaging approximately 2,500 Gm. in weight, and of the same stock used in previous experiments in this series, were inoculated in the anterior chamber of the right eye with 0.1 cc. of a six week culture of a virulent human strain of Mycobacterium tuberculosis, diluted so as to contain approximately 5 organisms to each oil immersion field. The rabbits were examined at weekly intervals, and the degree of tuberculous activity was estimated on a numerical scale (0 to 4), just as in previous experiments in this series. Within three weeks after inoculation all rabbits showed the development of characteristic early inflammatory lesions of experimental ocular tuberculosis.

Three weeks after inoculation the animals were divided into four groups of 16 rabbits each, the groups having almost equal average estimated degrees of tuberculous activity, and treatment was started. Group 1 was left untreated as a control. Group 2 was given paraaminosalicylic acid alone. This was incorporated in the feed so that the pellets of food contained 5 per cent by weight of the substance. Group 3 was treated with paraaminosalicylic acid and streptomycin. Paraaminosalicylic acid was incorporated in the feed so that the pellets contained 5 per cent by weight of paraaminosalicylic acid. Each rabbit received 50 mg. of streptomycin per kilogram of body weight, given subcutaneously once daily. Group 4 was treated with thiazolsulfone and streptomycin. Thiazolsulfone was added to their feed so that the pellets contained 1 per cent by weight of the drug. Each rabbit received 50 mg. of streptomycin per kilogram of body weight, given subcutaneously once daily.

Treatment was continued for 88 days, and all four groups were observed for an additional 104 days. At the end of the experiment all remaining rabbits were killed and the inoculated eyes removed for further study. The eyes of approximately 50 per cent of each group were studied histologically, and the eyes of the remainder were studied bacteriologically. For the histologic studies, the enucleated eyes were fixed in Zenker's solution, sectioned and stained with hematoxylin and eosin. For the bacteriologic studies, the uveal tracts were removed aseptically and macerated individually in sterile sodium chloride solution. Each specimen was examined for tubercle bacilli by direct smear stained by the Ziehl-Neelsen method. Each specimen was cultured on Dubos and Löwenstein's medium for tubercle bacilli. In addition, 0.1 cc. of each uveal tract suspension was injected into the anterior chamber of a healthy normal rabbit, and the animal was observed for the development of visible signs of ocular tuberculosis.

CLINICAL COURSE

The clinical courses of the four groups are shown in graphic form in figure 1, in which the average of the estimated inflammatory activity for each group is plotted against time, in weeks.

The untreated group ran the usual course of experimental ocular tuberculosis. The inoculated eyes showed progressive signs of inflammation, with development of tubercles of the iris and cornea, progressing into massive caseation and necrosis, with eventual buphthalmos and, in most cases, rupture of the globe.

The treated groups showed an entirely different course. For two to three weeks after the beginning of treatment the signs of tuberculous inflammation continued to increase, although this increase was not as great as in the untreated group. The treated groups all reached their maximum average activity about three weeks after the start of treatment and thereafter showed progressive decrease in activity. The groups receiving streptomycin and thiazolsulfone, and streptomycin and paraaminosalicylic acid showed a maximum tuberculous activity that was considerably less than that shown by the group receiving paraaminosalicylic acid alone. About four weeks after the start of treatment, the inoculated eye began to show less ciliary congestion, and there was healing of the cornea and iris tubercles. As can be seen in figure 1, this decrease in inflammatory activity occurred sooner, and the decrease

was more marked in the groups receiving streptomycin and paraaminosalicylic acid, and streptomycin and thiazolsulfone, respectively, than in the group receiving paraaminosalicylic acid alone. Nevertheless, the group treated with paraaminosalicylic acid alone showed a striking difference as compared with the control group.

Seven weeks after the start of treatment, six rabbits in group 3 (streptomycin and paraaminosalicylic acid) and eight rabbits in group 4 (streptomycin and thiazolsulfone) had eyes that were white and entirely free of visible active tuberculous inflammation. None of the rabbits in group 2 (paraaminosalicylic acid alone) had eyes without signs of active inflammation.

At the completion of treatment all the rabbits receiving streptomycin and thiazolsulfone (group 4) had eyes completely free of active inflammation, and all but one of the group receiving streptomycin and paraaminosalicylic acid were likewise free of activity. In the group treated with paraaminosalicylic acid alone, only four animals had eyes completely free of visible inflammation.

During the 104 day period of observation following termination of treatment, there were no recurrences of clinically visible signs of inflammation in any of the

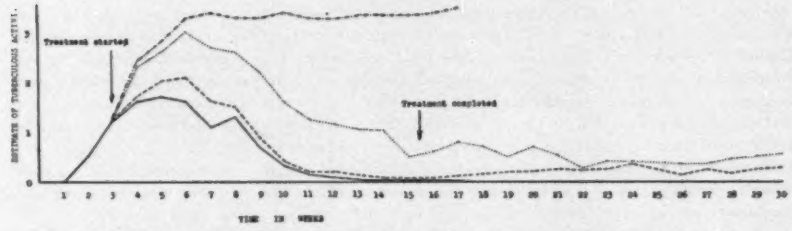

Fig. 1.—Effect of paraaminosalicylic acid, streptomycin and paraaminosalicylic acid, and streptomycin and thiazolsulfone on the clinical course of experimental ocular tuberculosis in normal rabbits. Tuberculous activity for untreated rabbits is indicated by a line of dots and dashes; that for rabbits treated with paraaminosalicylic acid alone, by the line of dots; that for rabbits treated with paraaminosalicylic acid and streptomycin, by the line of dashes, and that for rabbits treated with streptomycin and thiazolsulfone, by the solid line.

eyes in the group treated with streptomycin and thiazolsulfone. There were two definite recurrences in the group that had received streptomycin and paraaminosalicylic acid (rabbits 726 and 732), and five other animals (rabbits 725, 733, 735, 749 and 734) showed minimal or questionable activity at the time they were killed. There were seven animals in this group which showed no signs of any visible inflammatory activity during the period of observation.

In the group receiving paraaminosalicylic acid alone there were no definite recurrences, and at the time they were killed there were seven animals with eyes that showed no signs of active inflammation.

All animals were weighed at frequent intervals during the course of treatment. During the 88 days of treatment, the control group showed an average gain in weight of 8 per cent, while the group receiving streptomycin and thiazolsulfone showed a gain of 5 per cent. The two groups receiving paraaminosalicylic acid

showed an average loss of weight. The group which received paraaminosalicylic acid alone showed an average loss of 7 per cent, while the group receiving paraaminosalicylic acid and streptomycin showed an average loss of 2.5 per cent.

During the first four weeks of treatment six rabbits died—three in group 2 (paraaminosalicylic acid), one in group 3 (streptomycin and paraaminosalicylic acid) and two in group 4 (streptomycin and thiazolsulfone). There were no other deaths during the course of the experiment.

One animal (rabbit 715) in group 4 (streptomycin and thiazolsulfone) was noted to have gross evidence of severe vestibular dysfunction 77 days after the start of treatment. This persisted throughout the course of the experiment.

TABLE 1.—*Results of Studies for Presence of Tubercle Bacilli in Eyes Enucleated at Termination of Experiment*

Type of Treatment	Rabbit No.	Estimate of Tuberculous Activity at Time of Kill	Direct Smear of Uveal Tract	Culture of Uveal Tract	Transmission to Normal Eye
Group 1 (untreated)	702	4.0	+	+	+
Group 2 (paraaminosalicylic acid)	731	0.5	−	+	+
	744	2.0	+	+	+
	745	0.25	+	+	+
	751	0.0	−	−	−
	753	0.25	−	+	+
	774	0.50	−	+	+
Group 3 (paraaminosalicylic acid and streptomycin)	725	0.5	−	+	+
	726	3.0	+	+	+
	732	2.0	+	+	+
	733	0.5	−	+	−
	735	0.5	−	+	+
	749	0.25	−	+	−
	771	1.5	−	+	−
Group 4 (streptomycin and thiazolsulfone)	711	0.0	−	+	+
	715	0.0	−	−	−
	717	0.0	−	+	+
	718	0.0	−	−	−
	720	0.0	−	−	−
	721	0.0	−	−	−
	722	0.0	−	−	−

Paraaminosalicylic acid levels of the blood were determined in a number of instances during the period of treatment with the drug. These were found to average approximately 6 mg. per 100 cc. in the group receiving paraaminosalicylic acid alone and in the group receiving streptomycin and paraaminosalicylic acid.

BACTERIOLOGIC STUDIES FOR PRESENCE OF TUBERCLE BACILLI

The results of the various bacteriologic studies for the presence of tubercle bacilli in the inoculated eyes removed at the termination of the experiment are shown in table 1. In addition, this table shows the clinical estimate of tuberculous activity just prior to the time the animals were killed.

Five of six rabbits treated with paraaminosalicylic acid alone (group 2) whose eyes were cultured showed the presence of viable tubercle bacilli in the inoculated eyes. The animal in which tubercle bacilli were not isolated was the only one whose eye had appeared completely inactive prior to the time of being killed.

All seven of the animals treated with paraaminosalicylic acid and streptomycin (group 3) whose eyes were cultured showed the presence of viable tubercle bacilli. All these animals had shown visible signs of active inflammation just prior to being killed.

TABLE 2.—*Sensitivity to Streptomycin of Tubercle Bacilli Recovered from Inoculated Eyes at Termination of Experiment*

Type of Treatment	Rabbit No.	Sensitivity to Streptomycin in Micrograms per Cc.
Untreated group	702	1.56
Paraaminosalicylic acid	731	3.1
Paraaminosalicylic acid and streptomycin	725	3.1
	730	3.1
	732	3.1
	735	3.1
Streptomycin and thiazolsulfone	711	3.1
	717	3.1

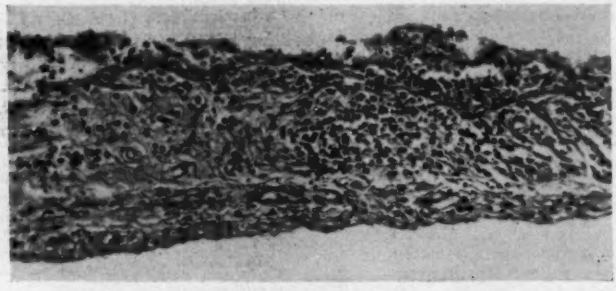

Fig. 2 (group 2).—Lymphocytic infiltration of the iris.

Only two of the seven animals treated with streptomycin and thiazolsulfone (group 4) whose eyes were cultured showed the presence of viable tubercle bacilli. However, all the eyes in this group had appeared entirely quiescent just prior to the time of killing.

The sensitivity to streptomycin of the tubercle bacilli isolated from the inoculated eyes was determined in a number of cases. These are shown in table 2. In every case tested, the tubercle bacilli showed no significant increase in resistance to streptomycin. Two of the rabbits tested (rabbits 726 and 732) were rabbits which had shown definite evidence of clinical recurrence after termination of treatment.

HISTOLOGIC STUDIES FOR PRESENCE OF TUBERCULOUS INFLAMMATION

Twenty of the inoculated eyes of rabbits from the three treated groups were examined histologically. These included five eyes in the group treated with paraaminosalicylic acid, eight eyes in the group treated with paraaminosalicylic acid and streptomycin and seven eyes in the group treated with streptomycin and thiazolsulfone. Immediately prior to killing, all these eyes were completely free of visible evidence of active inflammation, with the exception of rabbit 734, of group 3

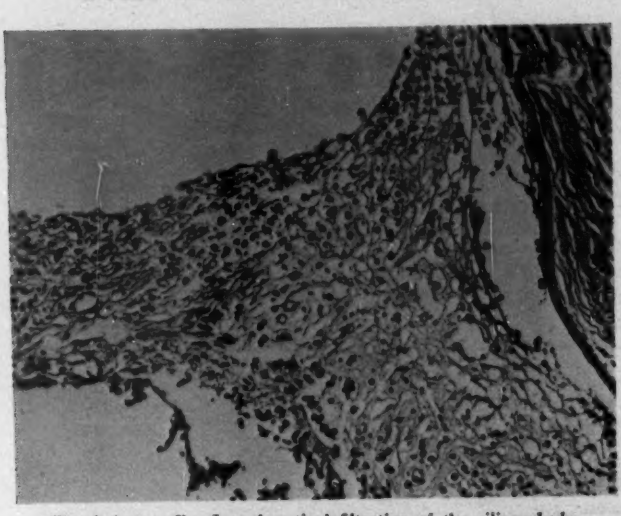

Fig. 3 (group 2).—Lymphocytic infiltration of the ciliary body.

Fig. 4 (group 2).—Tubercle of the cornea.

Fig. 5 (group 3).—Lymphocytes in the ciliary body.

Fig. 6 (group 4).—Clump of lymphocytes in the ciliary body.

(paraaminosalicylic acid and streptomycin). This eye showed minimal signs of inflammatory activity.

Two of the five eyes in group 2 (paraaminosalicylic acid) were free of histologic signs of active tuberculous inflammation. Two others (rabbits 752 and 772) showed only moderate lymphocytic cell infiltration in the iris and ciliary body, as shown in figures 2 and 3. Rabbit 755 showed tubercles of the cornea (fig. 4) and ciliary body, as well as a good deal of lymphocytic infiltration in the iris and ciliary body.

Two of the eight eyes examined histologically in group 3 (paraaminosalicylic acid and streptomycin) showed evidence of minimal active inflammation, while the remaining six eyes showed only an occasional isolated lymphocyte in the iris or ciliary body. Rabbit 728 showed a large clump of lymphocytes in the ciliary body (fig. 5) and scattered lymphocytes in the iris and ciliary body. Rabbit 739 showed moderate lymphocytic infiltration of the iris and ciliary body.

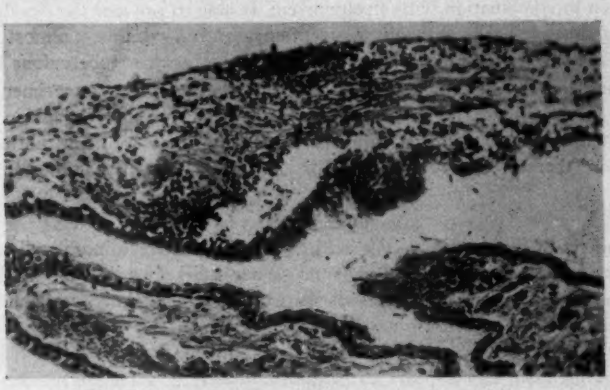

Fig. 7 (group 4).—Clump of lymphocytes in the iris.

Two of the seven eyes examined histologically in group 4 (streptomycin and thiazolsulfone) showed evidence of minimal active inflammation, while the remaining five eyes showed only an occasional isolated lymphocyte in the iris and ciliary body. Rabbit 727 showed a large collection of lymphocytes in the ciliary body (fig. 6), while rabbit 743 showed clumps of lymphocytes in the iris (fig. 7).

COMMENT

Under the conditions of this experiment, paraaminosalicylic acid showed a pronounced deterrent effect on the clinical course of experimental ocular tuberculosis in normal rabbits. Whereas the control group showed progressive tuberculous inflammation, which ultimately destroyed the inoculated eyes, the group treated with paraaminosalicylic acid showed arrest of the destructive tuberculous inflammation, leaving intact eyes either with no active inflammation or with signs of slight active inflammation. The combination of streptomycin and paraaminosalicylic acid showed a much greater deterrent effect than paraaminosalicylic acid alone, and in the dose chosen for this experiment was approximately as effective as a combination of streptomycin and thiazolsulfone.

The difficulty of completely eradicating the tubercle bacilli from an infected eye is emphasized by the high percentage of cases in which tubercle bacilli were isolated. Of the 20 treated animals whose uveal tracts were examined bacteriologically, tubercle bacilli were found by direct smear in 4, by inoculation of the anterior chamber in 11 and by culture in 14. Six eyes showed no tubercle bacilli in any of the tests. Two of the eyes from which cultures of tubercle bacilli were obtained appeared entirely inactive clinically, while 12 of the eyes from which positive cultures were obtained showed slight visible signs of active inflammation.

Further evidence of the insidious nature of the tuberculous process was shown by the demonstration of histologically active tuberculous inflammation in eyes that appeared clinically quiescent.

The failure of any of the tubercle bacilli recovered from treated eyes to show greatly increased resistance to streptomycin was striking. This finding is in agreement with other workers who have found that thiazolsulfone or paraaminosalicylic acid, given in combination with streptomycin, is able to prevent the development of strains of tubercle bacilli resistant to streptomycin. Indeed, this is a most important reason for using two or more drugs in combination against tuberculous infections.

It has been shown previously that the deterrent effect on experimental ocular tuberculosis is greater for a given dose of chemotherapeutic agent in immune-allergic animals than in normal animals. This experiment utilizing normal rabbits constitutes, therefore, a severe test for the efficacy of paraaminosalicylic acid.

SUMMARY

The effect of paraaminosalicylic acid alone, and of paraaminosalicylic acid combined with streptomycin, on experimental ocular tuberculosis in the normal rabbit is presented. Under the conditions of the experiment, paraaminosalicylic acid has been found to have a definite and deterrent effect on the course of experimental ocular tuberculosis. In combination with streptomycin, the deterrent effect is much more striking than, and appears to be approximately as effective as, the combination of streptomycin and thiazolsulfone (promizole®).

PATHOGENESIS OF OPHTHALMOPLEGIC MIGRAINE

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THE PROBLEM of the origin of the ocular paralyses occurring in the course of migraine, referred to as ophthalmoplegic migraine, remains unsolved. Of the several concepts which have been proposed to explain them, that of cerebral aneurysm has received wide acceptance, though there has been little evidence to support it. In order to test the validity of the concept of cerebral aneurysm as a cause of ophthalmoplegic migraine, two patients with this condition were studied by means of arteriography. In neither instance was an aneurysm demonstrated.

REPORT OF CASES

CASE 1.—*M. R. (J. H. no. R-54069). Recurrent pain in left side of head and left eye associated with ptosis of left eyelid, diplopia and partial oculomotor paralysis. Normal left internal carotid arteriogram on two occasions (1948 and 1950). No evidence of aneurysm to account for ophthalmoplegic migraine.*

The patient, a white woman aged 56, first appeared for relief on Oct. 26, 1948 with the complaint that she had pain in the left eye. She had suffered from periodic attacks of headache over the left side of the head for 22 years. These occurred at irregular intervals and were characterized by severe headache, vomiting and photophobia, lasting for 12 hours to two days. Her first episode of ophthalmic pain developed three years previously (1945), when she experienced sudden severe pain in the left eye, lasting three days. The pain at this time was confined to this eye and was associated with ptosis of the left eyelid. She was free of pain until six months later, when she again experienced severe pain deep in the left eye, spreading this time to involve simultaneously the left eyebrow, the bridge of the nose and a small area over the left frontal region. The episode on this occasion lasted six to eight days and was followed up to the time of her first examination by other headaches of a similar character but of varying intensity. At the time of her original examination the patient had had three episodes of headache in three weeks. Milder headaches incapacitated her for two to three days, and the severer attacks, for six to eight days. The latter were associated with nausea and vomiting and with ptosis of the left eyelid and diplopia, both of which disappeared after the cessation of the headache, usually within 24 hours, or sometimes 48 hours. The severe attacks were associated with suboccipital headache, as well as headache in the areas mentioned. There were no other factors of significance in the history except a cholecystectomy five years previously (1943) and a reported episode of coronary thrombosis one year previously, requiring bed rest for six months. The patient's mother was reported to have suffered from migraine, but there was no history of migraine in other members of her family or in her four children.

Examination (October 26) revealed adiposis dolorosa, with heavy accumulations of fat over the pelvic girdle and lower limbs distributed in characteristically lumpy fashion and with distinct tenderness in many parts. At the time of examination she was suffering from a mild headache, but no evidence of abnormality of the central nervous system could be detected.

From the Department of Neurology, Jefferson Medical College of Philadelphia.

The patient was admitted to the Jefferson Medical College Hospital on Nov. 10, 1948, for determination of the cause of her headaches, and was discharged on November 24. She was quite comfortable on this occasion and revealed no ptosis or other evidence of cranial nerve palsies. The urine and routine blood count were normal. The Wassermann and Kahn reactions of the blood were negative. The spinal fluid pressure was 150 mm. of water; the protein content, 50 mg. per 100 cc.; the Wassermann reaction, negative, and the colloidal gold curve, 0000000000. Roentgenograms of the chest and skull were normal. Electrocardiographic examination revealed a conduction deformity of the entire ventricular complex, produced by a left bundle branch block. Internal carotid arteriography revealed no evidence of aneurysm (fig. 1).

After her discharge from the hospital, the patient was relatively well for two months, until January 1949, when she had pain on the right side of the head, lasting only two days. This was followed 11 days later by headache on the left side, lasting six days, which she said was as severe as she had ever experienced, and which was associated with a condition described as swelling over the left side of the forehead. After this brief episode the patient was well until

Fig. 1 (M. R.).—Normal left internal carotid arteriogram performed on Nov. 17, 1948.

May 1950, about 16 months after the last episode of pain in the head and eye, when she experienced pain in the left eye and over the left frontotemporal region. It was described as sharp and throbbing and was associated with noticeable ptosis of the left eyelid. Nausea was constant, and vomiting was frequent throughout the period of headache. Double vision was present on lifting the left eyelid. The headache was constant for eight weeks and gradually disappeared.

Examination (May 23) revealed three-fourths ptosis of the left eyelid, without evidence of edema, and weakness of internal and upward rotation of the left eyeball. Repeated examinations revealed a similar condition. The patient was hospitalized in June 1950 because of persistent headache.

The urine was normal except for occasional red blood cells in two specimens, not noted in the many subsequent specimens, and a trace of albumin on two occasions. The specific gravity varied from 1.005 to 1.010. The routine examination of the blood showed a normal condition. Examination of the spinal fluid revealed a pressure of 135 mm. of water, 4 cells per cubic millimeter, a protein content of 50 mg. per 100 cc., a negative Wassermann reaction and a colloidal

gold curve of 0000000000. Roentgenograms of the skull showed nothing abnormal, but those of the chest revealed slight cardiac enlargement and "some scoliosis and uncoiling of the aortic arch." The left internal carotid arteriogram was normal (fig. 2).

Summary.—The patient first had episodes of ophthalmoplegic migraine on the left side at the age of 53. She had no history of migraine earlier in life, but her mother was reported to have suffered from migraine. The pain was centered in the left eye but extended into the left frontotemporal region and was associated with partial oculomotor paralysis on the same side, as indicated by diplopia, ptosis of the left eyelid and weakness of internal and upward rotation of the left eyeball. Laboratory studies revealed nothing abnormal. Internal carotid arteriograms performed in 1948 and again in 1950 revealed no evidence of aneurysm to account for the ophthalmoplegic migraine. The symptoms were such that if aneurysm had been present it would have been revealed in the arteriograms.

Fig. 2 (M. R.).—Normal left internal carotid arteriogram performed on June 5, 1950.

CASE 2.—*H. S. (J. H. no. 1H-12060), a woman aged 23. Recurrent episodes of headache associated with ptosis of left eyelid and diplopia, characteristic of ophthalmoplegic migraine. Failure to disclose aneurysm by arteriography and operation. Death following arteriography.*

The patient, a woman aged 23, was first admitted to the Jefferson Medical College Hospital on March 22, 1946 with a history of recurrent episodes of occipital and frontal headache, at times associated with drooping of the left upper eyelid and diplopia on looking to the left side. She had noticed that her left eyelid drooped slightly in the past year when she had headache. The headache was in the occipital region but was frequently located also in the frontal area above the left eye. The pain was sharp and tended to be persistent, at times persisting three to four hours. About one month prior to her admission, the left eyelid drooped more than usual, and the patient noted that at times she had diplopia on looking to the left. She also supplied the information that for six months prior to admission the headaches, especially over the frontal area of the scalp, seemed to become progressively frequent and persistent. The headaches were not relieved by acetylsalicylic acid and were aggravated when she turned her head suddenly to one side or the other.

Physical and neurological examinations on admission revealed only slight ptosis of the left eyelid. The Wassermann and Kahn reactions of the blood were negative. Chemical and routine studies of the blood revealed nothing abnormal. Spinal puncture yielded clear fluid under an initial pressure of 130 mm. of water, with 3 cells per cubic millimeter and a protein content of

31 mg. per 100 cc. The Wassermann reaction of the spinal fluid was negative. Roentgenograms of the skull revealed nothing abnormal. An encephalographic study performed on April 1, 1946 showed nothing significant. The visual fields were normal.

In order to exclude myasthenia gravis, 4 cc. of 1:2,000 neostigmine methylsulfate was given intramuscularly. No objective or subjective improvement was noted 40 minutes after the injection. The headache disappeared and the ptosis receded, the patient experiencing a spontaneous remission while in the hospital, similar to that which she had experienced a number of times in the six months before hospitalization.

After discharge the patient was troubled by recurrent frontal and occipital headaches, which were controlled by acetylsalicylic acid, with no recurrence of the ptosis. One year prior to her second admission a friend remarked to her that the pupil of the left eye was very much dilated. The next day, while riding in a car, she suddenly experienced a sharp, lancinating pain in her left eye, her vision became blurred and she stated that the pain at the time was almost unbearable. Examination revealed ptosis of the left eyelid and extreme dilatation of the left pupil. The pupil responded sluggishly to light and in accommodation. The pain continued and was localized

Fig. 3 (M. S.).—Normal left internal carotid arteriogram.

behind the left eye and over the left supraorbital ridge. Neurological examination failed to reveal other objective signs at this time. Study of the visual fields revealed no defects. Visual acuity was normal in both eyes. Roentgenograms of the skull showed a normal condition. Lumbar puncture was performed, and clear, colorless fluid was obtained, under an initial pressure of 100 mm. of water. The Wassermann reaction of the spinal fluid was again negative. The spinal fluid protein was found to be 32 mg. per 100 cc.

As on her previous admission, the presence of an intracranial aneurysm was suspected. On April 2, 1947 the left internal carotid artery was injected with a 35 per cent iodopyracet (diodrast®) solution by Dr. Rudolph Jaeger. The left internal carotid artery was dissected, and under x-ray visualization it was injected with 10 cc. of 35 per cent iodopyracet solution. Stereoscopic views were taken by repeating the procedure, a total of 20 cc. of the iodopyracet solution being used. No aneurysm was detected (fig. 3). The patient remained stuporous after the arteriographic procedure. The next day a craniotomy was performed on the left side. A bone flap was turned down to expose the bases of the frontal and temporal lobes. The large Sylvian veins were coagulated and cut from the sphenoid ridge. The temporal and frontal lobes were easily lifted so as clearly to expose the entire base of the brain on the left side. The optic chiasm

and the left internal carotid artery and posterior cerebral arteries were entirely normal. The ophthalmic artery was identified and found normal in position. The anterior cerebal arteries appeared normal. The third nerve was explored for a distance of 1 inch (2.5 cm.) and was observed to pass out beneath the edge of the tentorium without evidence of a gross lesion. Exposure of all basal structures was exceedingly good, and there seemed to be little possibility of overlooking an aneurysm. The wound was tightly closed with silk sutures after the bone flap had been wired in place. The patient remained stuporous, and it was noted that her left arm was paralyzed. Twenty-four hours after the craniotomy the patient was still stuporous and was found to have left hemiplegia. Her stupor continued; she finally became comatose and died 48 hours after her operation.

Autopsy revealed thrombosis of the left internal carotid artery. The Sylvian vessels on the left side were also occluded. The sagittal sinus of the dura was patent. There was an extradural hematoma measuring 5 cm. The convolutions of the hemispheres were flattened bilaterally, and there was herniation beneath the falx of the medial surface of the left hemisphere. The uncus was herniated on the left. Coronal sections of the cerebrum revealed edema, with softening and pink discoloration of the cortex of the left hemisphere, including the first, second and third frontal convolutions within a short distance posterior to the frontal pole. The white matter in the left hemisphere was soft and edematous, as was the anterior superior portion of the caudate nucleus, the putamen and the anterior limb of the internal capsule. In the medial segment of the globus pallidus was a small area of cystic softening. Sections of the brain stem and cerebellum revealed no gross lesions.

Microscopic study of sections of the cerebral cortex revealed extensive destructive changes within the distribution of the middle cerebral artery. These consisted of swelling, coagulation necrosis, loss of nerve cells and early regressive changes in the astrocytes, with no well developed gitter cell formation or lysis of tissue. These changes had an over-all distribution corresponding to the areas of the brain supplied by the left middle cerebral artery. There were numerous thrombosed vessels, usually occurring in groups and surrounded by hemorrhage in these areas, and large numbers of polymorphonuclear leukocytes. The latter cells occurred free in the tissue in great profusion. The superior portion of the head of the left caudate nucleus, the superior portion of the left anterior limb of the internal capsule, the anterior portion of the putamen and the superior two thirds of the globus pallidus, and the external capsule and the island of Reil revealed changes similar to those noted in the cerebral cortex. Microscopic study of the brain stem revealed nothing abnormal. The neuropathological diagnosis was occlusion of the left internal carotid artery, with softening of the cerebral cortex and basal ganglions, chiefly in the distribution of the left middle cerebral artery.

Summary.—A woman, aged 23, suffered recurrent headaches associated with ptosis of the left eyelid and with diplopia on looking to the left side. Examination during the course of such episodes revealed ptosis of the left eyelid and a dilated left pupil with a very sluggish light reaction. She was regarded as having an ophthalmoplegic type of migraine with aneurysm formation of the left internal carotid or posterior communicating artery. An arteriogram of the left internal carotid artery failed to reveal an aneurysm. Exploration disclosed no aneurysm. Thrombosis of the left internal carotid artery with left hemiplegia developed after arteriography. The patient died 48 hours after operation. Autopsy revealed no evidence of aneurysm.

COMMENT

Clinical Features.—Ophthalmoplegic migraine is characterized by paralysis of ocular muscles, occurring during an attack of migraine, or at times developing without an attack of headache in a patient subject to migraine. In the majority of instances the oculomotor nerve is affected, but isolated instances of trochlear and abducens paralysis have been observed. In oculomotor involvement, there may develop both internal and external ophthalmoplegia, but in some instances only internal ophthalmoplegia may occur, with resulting dilatation of the pupil and

loss of accommodation. In rare instances paralysis of convergence and divergence may result (Marlow [1]). "The commonest ocular muscle paralysis occurring in conjunction with migraine is a total or partial paralysis of the muscles supplied by the third nerve, with or without involvement of the pupil" (Donahue [2]). Donahue stated that cases of internal ophthalmoplegia are infrequent and that only a single branch of the oculomotor nerve may be affected, for example the branch to the levator palpebrae. He asserted further that numerous cases of complete external ophthalmoplegia have been recorded but that isolated paralysis of the trochlear nerve is rare. Riley [3] stated that the lens curvature may pass through different phases during the attack, an object looked at alternately becoming indistinct, out of focus and then definite and clear. Though Gubler [4] was the first to record a description of this syndrome, it was Saundby,[5] in 1882, who first appreciated its nature when he described a patient with attacks of "megrim and paralysis of the third nerve." The term "ophthalmoplegic migraine" was suggested by Charcot [6] in 1890, and the syndrome was mentioned by Möbius [7] in 1894 as a periodic recurrent paralysis of the ocular muscles associated with headache and vomiting.

Since 1894 numerous reports have appeared substantiating the belief that ophthalmoplegic migraine is a distinct entity occurring during the course of migraine. Despite this impression, there are features of the condition which raise doubt as to whether the ophthalmoplegic form is identical with typical migraine. The term ophthalmoplegia migraine requires careful definition. With its use as a purely descriptive term to indicate those cases of migraine associated with ophthalmoplegia there appears to be little quarrel. Inferences which extend beyond this usage, however, give rise to important differences. The syndrome is regarded by some as identical with migraine, resulting from the same mechanisms as those which are responsible for the typical migraine headache. By others, ophthalmoplegic migraine is regarded as the result of secondary factors which are unassociated with the migraine itself and which must be regarded as purely fortuitous. This viewpoint was clearly expressed by Riley,[8] who stated:

> . . . All of the recorded cases of ophthalmoplegia with headache should be looked upon as cases of ophthalmoplegia with headache, but not as constituting a separate form of migraine. . . . In every instance in which the patient has shown attacks of ophthalmoplegic disturbances associated with headache, and has come to postmortem investigation, there has always been found some element of pathological character which interfered with the function of the particular nerve involved.

The few cases with autopsy available for study support this contention, provided one is willing to accept the findings reported as responsible for the attacks of

1. Marlow, F. W.: Ophthalmoplegic Migraine: Convergence Paralysis, Am. J. Ophth. **11**:222, 1928.

2. Donahue, H. C.: Migraine and Its Ocular Manifestations, Arch. Ophth. **43**:96 (Jan.) 1950.

3. Riley, H. A.: Migraine, Bull. Neurol. Inst. New York **2**:429, 1932.

4. Gubler, A.: Des paralysies consecutivés aux maladies aiguës, Gaz. hôp. **33**:58, 1860.

5. Saundby, R.: A Case of Megrim, with Paralysis of the Third Nerve, Lancet **2**:345, 1882.

6. Charcot, J. M.: Sur un cas de migraine ophthalmoplégique, Progr. méd., Paris **1**:89, 1890.

7. Möbius, P. J.: Die Migraine, Vienna, A. Hölder, 1894. Nothnagel, H.: Handbuch der speciellen Pathologie und Therapie, Leipzig, F. C. W. Vogel, 1899, vol. 12, pt. 2.

8. Riley, H. A., in discussion on Kennedy, F.: A Case of Ophthalmoplegic Migraine, and a Theory for Its Production, J. Nerv. & Ment. Dis. **104**:89, 1946.

ophthalmoplegia. On the other hand, the absence of specific lesions in many cases of ophthalmoplegic migraine has given rise to the belief that the cases included in this category can be divided into two groups: those with and those without specific causes for the ophthalmoplegia. Bürki,[9] in accordance with this concept, divided the cases of ophthalmoplegic migraine into two groups: (1) those of the essential form, in which no cause is found, and (2) those of the symptomatic form, characterized by structural changes of various kinds, chief among which is aneurysm. The case for aneurysm was supported by Wolff,[10] who stated that "it would appear that at least some of the patients described as having ophthalmoplegic migraine had cerebral aneurysms pressing on the third, and perhaps other, cranial nerves." He stated, moreover, that "at least in some instances ophthalmoplegic migraine is the result of pressure exerted by greatly dilated, thickened, or edematous arterial walls, associated with migraine headache attacks—which obviously would not be demonstrable in postmortem examination."

Ophthalmoplegic migraine pursues a clinical course usually divided into two periods. There first occurs the period of pain, followed by ophthalmoplegia. The pain begins abruptly and is localized deep behind the eye, in the eye itself, just over the eye or, less commonly, over the temple on that side. In most of the reported cases the pain is nearly always confined to the one side. Only occasionally has the headache been reported as bilateral. If the headache continues and becomes severer, nausea and vomiting may occur. Occasionally, dizziness has been reported in association with the headache. With the subsidence of the headache there appears the second period of the syndrome, or the period of paralysis. In the great majority of cases the appearance of paralysis coincides with the subsidence of headache, although in many instances the headache and the paralysis of the oculomotor muscles appear at the same time. The ophthalmoplegia may make its appearance during the attack or from one to ten days after the cessation of the headache. Möbius,[7] in an analysis of 29 cases of ophthalmoplegic migraine, found that in 7 of 11 of these cases the two symptoms, headache and ophthalmoplegia, made their appearance simultaneously, and that in 4 cases one symptom developed at a later date than the other. The ophthalmoplegia itself has typical characteristics which are present in the majority of cases, although exceptions may occur. It is usually confined to the oculomotor nerve, involvement of which may be complete or partial, affecting various combinations of muscles supplied by this nerve. In many instances the paralysis affects both the internal and the external musculature. The internal musculature may be involved alone, with only a dilated pupil as evidence of its implication. Convergence movements may be paralyzed on the involved side. Occasionally one of various combinations of involvement of the oculomotor, trochlear and abducens nerves is found, and rarely all these nerves may be involved, resulting in complete external ophthalmoplegia. Involvement of the trochlear or abducens nerve is rare in ophthalmoplegic migraine, but Leizenberger[11] reported the case of a man, aged 29, who had migrainous attacks every eight days, followed by isolated paralysis of the trochlear nerve. When the trochlear nerve is involved, it

9. Bürki, E.: Zur Kenntnis der ophthalmoplegischen Migräne, Confinia neurol. 4:54, 1941.

10. Wolff, H.: Headache and Other Head Pain, New York, Oxford University Press, 1948, pp. 390-395.

11. Leizenberger, cited by Posey, W. C., and Spiller, W. G.: The Eye and the Nervous System, Philadelphia, J. B. Lippincott Company, 1906.

is usually affected in association with the oculomotor nerve, as in the case recorded by Coutouzis,[12] in which the associated paralysis of the oculomotor and trochlear nerves occurred in the presence of violent headache. Paralysis of the abducens nerve has been recorded in a few instances (Hunt [13]).

The duration of the period of pain and of the period of paralysis varies. The period of pain is usually shorter than that of the paralysis, which may last from a few days to many months, usually with complete restoration of function. In the reported cases it is usually two days to two weeks before function of the extraocular muscles returns to normal. Möbius [7] found that in eight of 16 cases of the syndrome in his series, observed over a long period, there was either partial or complete persistence of some of the paralytic symptoms. It has been observed in some cases that after repeated attacks of ophthalmoplegic migraine the paralysis tends to persist for longer and longer periods and in time to become permanent. This sequence of events is especially true of those cases in which the period of the paralysis is prolonged and the attacks occur at frequent intervals. In such instances the intervals between the attacks are not always entirely free from the presence of some degree of paresis of the ocular muscles.

Möbius [7] and others have shown that the hereditary and familial factors are not nearly so prominent in the ophthalmoplegic form as in other types of migraine. Möbius pointed out that in his analysis of 29 cases of ophthalmoplegic migraine appearing in the literature he found a history of headache in some other member of the family in only four instances. The onset of migraine in cases of this syndrome is often at a very early age. Möbius found that in his series the onset was before 10 to 15 years of age in 6 cases and between the ages of 15 and 20 years in 2 cases.

There is often a change in the type of headache in the ophthalmoplegic form of migraine. In the early years the syndrome may appear as ordinary ophthalmic migraine associated with subjective sensory phenomena, such as scintillating scotoma or other subjective visual symptoms. This may change later to the ophthalmoplegic type. Chabbert [14] reported two sisters who had attacks of migraine associated with scintillating scotoma and hemianopsia. In one, at the age of 52, the attacks became complicated by paralysis of the right oculomotor nerve. Joachim [15] had a patient who was afflicted with ordinary ophthalmic migraine from his eleventh year; at 20 years of age oculomotor paralysis with diplopia developed suddenly after a slight attack of migraine.

Pathological Features.—Four cases of ophthalmoplegic migraine have been reported with autopsy. The case included in this report constitutes the fifth case on record.

Weiss [16] (1885) reported the case of a woman, aged 30, who since childhood had had repeated attacks of total paralysis of the left oculomotor nerve. During

12. Coutouzis: Nouvelle observation d'un cas de migraine ophthalmoplégique—paralysie du nerf oculo-moteur commun périodique, J. méd. et chir. prat. **68**:308, 1897.

13. Hunt, J. R.: A Contribution to the Paralytic and Other Persistent Sequelae of Migraine, Am. J. M. Sc. **150**:313, 1915.

14. Chabbert, L.: Sur un cas d'ophthalmoplégie nucléaire transitoire, consécutive à une migraine ophthalmique—ophthalmoplégie migraineuse, Progr. méd., Paris **23**:241, 1895.

15. Joachim: Über periodische Oculomotoriuslähmung, Deutsche Arch. klin. Med. **44**:185, 1889.

16. Weiss, D.: Ein Fall von periodisch auftretender totaler linkseitiger Oculomotoriuslähmung, Wien. med. Wchnschr. **35**:521, 1885.

the two months preceding her death she had two attacks, and during the month in which she died, a third, which lasted about three weeks. Autopsy revealed a number of gray granulations on the roots of the left oculomotor nerve as it emerged from the brain stem. The granulations were of sufficient size to produce warty swellings. Similar granulations were noted on the base of the brain, from which many tubercle bacilli were recovered. As others have already pointed out, the value of this case is doubtful in shedding light on the pathogenesis of ophthalmoplegic migraine. Though the ophthalmoplegic attacks occurred over a period of more than 20 years, the lesions found at autopsy were more recent.

Richter [17] (1887) reported the clinical and postmortem investigation of a patient who had had periodic recurrent paralysis of the right oculomotor nerve. The attacks were associated with headache and loss of appetite. The patient gave a history of a fall from a ladder at the age of 13 years, after which accident he was afflicted with convulsive seizures. The ophthalmoplegic attacks were characterized by loss of appetite, headache on the right side, mental depression, marked ptosis of the right eyelid, lacrimation and outward deviation of the right eye, with pronounced restriction of the right visual field for all colors. The involvement of the right oculomotor nerve was progressive and accompanied with loss of the reactions to light and in accommodation and convergence, together with ptosis, external strabismus and limitation of movement in all directions except upward. Death occurred shortly after the oculomotor paralysis became complete. At autopsy the right oculomotor nerve was observed to present a club-shaped enlargement as it passed through the dura mater, so that this part of the nerve was about twice the normal size. Circumscribed white deposits were noted on the blood vessels at the base, and the muscular coats of the vessels were reported as thickened. Microscopic examination revealed that the enlargement of the right oculomotor nerve was due to a fibrochondroma, which had separated the fasciculi of the nerve but had not destroyed them. There were no changes in the cells of the oculomotor nuclei, and all the muscles of the right eyeball were normal. Section of the optic nerve showed no abnormality. Richter stated that the tumor cells were deposited between the bundles of the oculomotor nerve and that they had effected no material change in the nerve itself. He suggested that a functional increase in the size of the tumor might from time to time cause an intermittent increase in pressure and thus interfere with the function of the nerve, at the same time causing headaches and reflex vomiting.

Karplus [18] (1895) reported the case of a woman, aged 43, with dementia paralytica. From the age of 6 months she had suffered from recurrent attacks of right-sided headache, vomiting and ophthalmoplegia, occurring every two to four weeks. The attacks appeared to be typical episodes of ophthalmoplegic migraine. She contracted syphilis at the age of 18 years, for which she was treated. In time permanent ptosis developed, with dilatation of the pupils and external strabismus. At autopsy, in addition to the evidences of parenchymatous syphilis of the brain, a neurofibroma about the size of half an almond was observed in the right oculomotor nerve. The fibers of the nerve were intertwined with strands of neoplastic tissue and revealed considerable degeneration.

17. Richter, A.: Ein Fall von typisch recidivirender Oculomotoriuslähmung mit Sectionsbefund, Arch. Psychiat. **18**:259, 1887.

18. Karplus, J. P.: Ophthalmoplegic Migraine with Autopsy, Wien. klin. Wchnschr. **8**:883, 1895.

Shionoya [19] (1911) reported the case of a 16 year old youth who had had attacks of migraine since he was 6 years old. The attacks occurred about once a month, were typically of the ophthalmoplegic type, involving the right eye, and usually lasted from seven to 10 days. He died of tuberculous meningitis. At autopsy widespread evidence of tuberculosis of the brain and meninges was found. In addition, the right oculomotor nerve presented a local thickening, as a result of which the nerve had attained a size about five times its normal diameter. Microscopic examination revealed the thickening to be due to heavy strands of connective tissue, deficient in blood vessels and nuclei. The surface of the nerve was covered with exudate and was infiltrated with round cells. The connective tissue strands were intimately intertwined with the nerve fasciculi, so that the usual arrangement of the latter was distorted. The myelin sheaths were in many instances badly damaged, but the axis-cylinders were fairly well preserved. There was no round cell infiltration of the nerve itself.

Cases of Ophthalmoplegic Migraine with Autopsy

Author	Clinical Features	Autopsy Findings
Weiss [16] (1885)	Complete paralysis of left oculomotor nerve; recurrent attacks 20 yr.	Warty granulations on left oculomotor nerve and over base of brain, in which tubercle bacilli found
Richter [17] (1887)	Paralysis of right oculomotor nerve, incomplete until shortly before death	Fibrochondroma involving right oculomotor nerve, with partial destruction of nerve
Karplus [18] (1895)	Complete paralysis of right oculomotor nerve; recurrent attacks 43 yr.	Neurofibroma of right oculomotor nerve and parenchymatous syphilis of brain
Shionoya [19] (1911)	Involvement of right oculomotor nerve; recurrent attacks 10 yr.	Tuberculous meningitis; right oculomotor nerve 5 times normal size, owing to connective tissue proliferation
Dassen [20] (1931)	Two attacks of paralysis of right oculomotor nerve	Aneurysm of right posterior communicating artery
Alpers and Yaskin (1951)	Incomplete paralysis of left oculomotor nerve	No aneurysm; nothing found at autopsy to account for oculomotor paralysis

Dassen [20] (1931) reported a case which he considered one of ophthalmoplegic migraine, with two attacks of paralysis of the oculomotor nerve, in the second of which death occurred. At autopsy the brain stem was observed to be completely surrounded by an extensive hemorrhage, which had filled the ventricle. In the vicinity of the left mamillary body a small aneurysm which had apparently ruptured, was found in the left posterior communicating artery.

Pathogenesis.—Relatively little light is thrown on the pathogenesis of ophthalmoplegic migraine by the cases studied at autopsy. It is probable that the reported findings were fortuitous and had little to do with migraine and its accompanying ophthalmoplegia.

In view of our present knowledge concerning the vascular mechanism of the migraine headache, it is hardly probable that the findings reported at autopsy are at all pertinent to the problem of ophthalmoplegic migraine. It is impossible to relate tumor involving the optic nerve, tuberculous infection and connective tissue

19. Shionoya, F.: Ein Fall von rezidivierender Oculomotoriuslähmung (Migraine ophthalmoplegique) mit Autopsie, Deutsche Ztschr. Nervenh. **42**:155, 1911.

20. Dassen, R.: Jaqueca oftalmopléjica con parálisis recidivante del III par craneano: Muerte en el segundo ataque; Necropsia, Semana méd. **51**:1049, 1931.

overgrowth involving the oculomotor nerve to recurrent episodes of ophthalmoplegic migraine. In the case of Dassen, in which an aneurysm involved the posterior communicating artery, only two acute episodes of headache and oculomotor paralysis occurred, and the case is much more likely one of an aneurysm primarily than of ophthalmoplegic migraine. The recurrent headache characteristic of migraine was conspicuously absent in this case.

Skepticism concerning the relation to ophthalmoplegic migraine of the autopsy findings in the recorded cases has been expressed by others who have dealt with the problem. Bramwell [21] suggested that the pathological lesions met with in the reported cases were not the cause, but the consequence, of the attack; that is, the lesions resulted from direct pressure on the nerve by an artery or by pressure on the nerve as a consequence of repeated traction as the nerve passed through the dura. He called attention to the anatomical relations of the oculomotor and abducens nerves to the arteries at the base of the skull. He stated that the oculomotor nerve lies immediately posterior to the posterior cerebral artery and that the abducens nerve occupies a similar position in relation to the tranverse artery to the pons. He regarded recurrent pressure on the nerves through dilatation of the arteries as the pathogenetic factor in the syndrome and explained the periodicity of the attacks by temporary distention of the artery or aneurysm, a consequence of vasomotor change, such as accompanies the migrainous paroxysm. Riley [3] also questioned the relation of the reported lesions to the recurrent attacks of headache unless it can be demonstrated that the oculomotor nerves contain, or are associated with, afferent fibers, irritation of which might cause the symptomatic syndrome characteristic of migraine. Ehlers [22] advanced the hypothesis that changes in the caliber of the posterior cerebral artery may account for the pathogenesis of this syndrome. The posterior cerebral arteries are the terminal branches of the basilar arteries. They run a curved course, laterally, in front of the oculomotor and trochlear nerves at the point where they advance toward the cavernous sinus. The position of the oculomotor nerve in the interpeduncular fossa makes it much more vulnerable to compression by this vessel than is the trochlear nerve. The posterior cerebral vessel runs backward and forms the sole vascular supply for the entire visual area in the calcarine cortex. Ehlers suggested that vascular changes in the occipital lobe are the cause of the various visual phenomena associated with ophthalmic migraine and that pressure of the same vessel on the oculomotor nerve could cause the motor paralysis seen in ophthalmoplegic migraine. Daily [23] likewise accepted the hypothesis advanced by Ehlers and expressed the belief that ophthalmoplegic migraine is a special type of the ophthalmic form of migraine and is secondary to vasomotor disturbances in the distribution of the posterior cerebral artery. Oppenheim [24] believed that either temporary spasm of vessels or temporary dilatation, with resulting anemia or compression, could account for the transitory paralysis

21. Bramwell, E.: Upon Leaking Aneurysm of Cerebral Arteries as Cause of Third Nerve Paralysis, with Special Reference to 2 Cases in Which Diagnosis Was Confirmed by Arterial Radiology: Note upon Aetiology of Recurrent and Periodic Ocular Palsy and Ophthalmoplegic Migraine, Tr. Ophth. Soc. U. Kingdom **54**:205, 1934.

22. Ehlers, H.: On Pathogenesis of Ophthalmoplegic Migraine, Acta psychiat. et neurol. **3**:219, 1928.

23. Daily, R. K.: Ophthalmoplegic Migraine, Texas J. Med. **36**:902, 1941.

24. Oppenheim, H.: Lehrbuch der Nervenkrankheiten, Berlin, S. Karger, 1908.

observed in this syndrome. He believed that repeated attacks would tend eventually to cause degenerative changes in the nerve, so that complete recovery failed to occur in some cases.

SUMMARY

The problem of ophthalmoplegic migraine presents great difficulties both in its clinical features and in its pathogenesis. It seems advisable from the clinical evidence at hand to regard it as a true entity occurring in some cases of migraine. There is no evidence to indicate why it occurs in some instances rather than in others. Whether it is a form of ophthalmic migraine is still not clear. It seems justifiable to regard it as a special form of migraine independent of the ophthalmic form, though there are instances, as Walsh [25] pointed out, in which the ophthalmic type develops later into true ophthalmoplegic migraine. There seems little justification to divide the ophthalmoplegic form into genuine and secondary forms. The latter is not migraine, but, rather, oculomotor paralysis associated with aneurysm or other form of organic disease. Though the clinical picture resembles that of ophthalmoplegic migraine, it differs in the absence of attacks of true migraine headache in the generally accepted sense of the term.

The few cases on record with autopsy fail to clarify the cause of the ophthalmoplegia in migraine. It is probable that some vascular disturbance is associated with the ophthalmoplegic attack, but its nature has not been defined. Neither the cases with autopsy nor the instances here recorded support the contention that cerebral aneurysm is responsible for the ophthalmoplegia. Vasomotor changes affecting the nerve (Ehlers) and recurrent pressure on the nerve by dilatation of the vessels in relation to the affected nerve (Bramwell) have been suggested as the cause of the oculomotor paralysis. The evidence in support of these hypotheses is far from conclusive, but in view of our present day understanding of the mechanism of migraine there appears to be some support for them.

25. Walsh, F. B.: Clinical Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947, p. 1308.

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistent with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

PECULIAR MACULAR LESIONS WITH UNACCOUNTABLY GOOD VISION

The following three cases show such remarkable similarities that we wish to report them together.

CASE 1 (seen by J. S. F.).—The patient, a healthy woman aged 42, had never had any serious illness. The trouble with her eyes was first discovered six years ago, when she consulted Dr. Warren C. Phillips, of Harrisburg, Pa. At that time the left eye was found to be entirely normal, while the right eye "showed a large oval orange-yellow lesion at the macula, about ¾ disk diameter in size." Vision with correction was 20/25 in the right eye and 20/20 in the left.

The patient was reexamined by Dr. Phillips in 1949, when the lesion in the right eye had grown to more than 1½ disk diameters and a similar lesion, approximately two-thirds the size of the disk was noted in the left eye. Visual acuity was then 20/50 + in the right eye and 20/20 + in the left eye.

Dr. Phillips reports that the patient's father had failing central vision beginning at the age of 40 and that when he was an old man he was reported to have had vision of 4/200 in the right eye and 15/200 in the left eye, with a large atrophic area in the macula of each eye.

The lesions as seen in 1950 are shown in figure 1. The sharply circumscribed, waxy, disk-shaped lesions appeared slightly elevated and were of a yellow or slightly orange creamy color.

CASE 2 (seen by A. E. M.).—The patient, a middle-aged man in good general health, complained of a recent decline in his vision. The ophthalmoscopic picture (fig. 2) presented in this case was almost identical with that in case 1. Visual acuity with correction was 20/40 in the right eye and 20/30 in the left eye.

CASE 3 (seen by A. E. M.).—The patient, a 13 year old boy, had no ocular complaints but was referred for routine examination by his teacher because of slight reduction of vision in his right eye. Visual acuity with correction was 20/40 —2 in the right eye and 20/20 in the left eye. The ophthalmoscopic picture (fig. 3) was similar to that of cases 1 and 2.

Comment.—No complete review of the literature has been made to discover whether similar cases have been reported previously, but there would seem to be no doubt that the condition presented in these three cases is an extremely rare one. All three patients were in excellent general health, and no evidence of systemic disease was discovered on routine examination. The possibility that the condition may be hereditary is suggested by the family history in case 1. This case also indicates that the lesion is slowly progressive. No scotoma in the central field could be mapped in any of these cases using ordinary perimetric targets.

Various suggestions as to the nature of the lesion have been entertained. Ophthalmoscopic examination clearly establishes that it is subretinal. The relatively small defect in visual acuity would seem to indicate that the choriocapillaris under

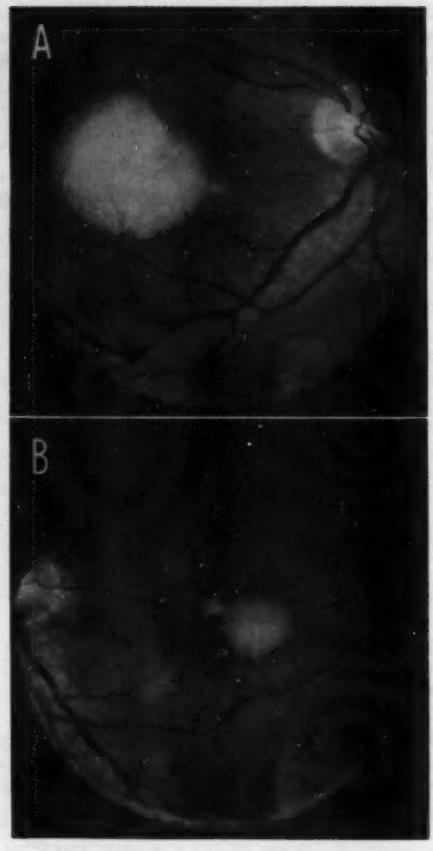

Fig. 1 (case 1).—*A*, right eye; *B*, left eye.

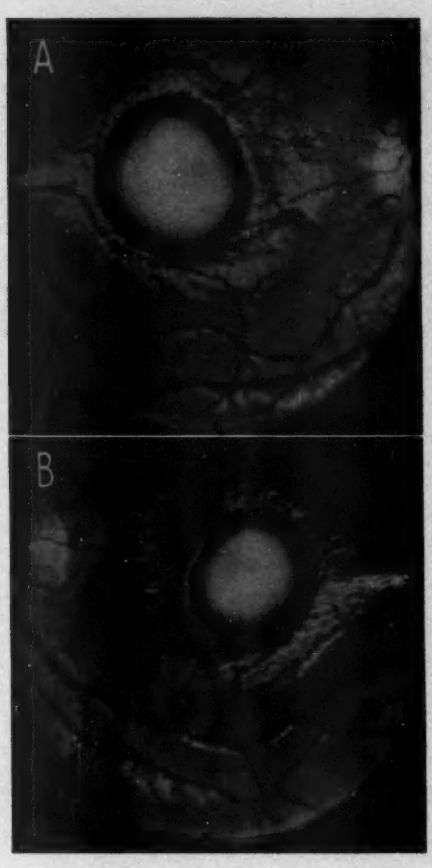

Fig. 2 (case 2).—*A*, right eye; *B*, left eye.

Fig. 3 (case 3).—Right eye.

the lesion is not severely disturbed. If the pigment epithelium is still present in the region of the lesion, it must either have lost its pigment or be covered by opaque material. In any case, we believe that the lesion lies somewhere between the choriocapillaris and the retinal cones. We have no suggestion as to the nature of the lesion except that it is clearly neither inflammatory nor neoplastic. The remote possibility that this lesion is analogous to the tapetum cellulosum of lower animals may be mentioned.

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STELLATE GANGLION BLOCK FOR CEREBROVASCULAR ACCIDENT INVOLVING HOMONYMOUS HEMIANOPSIA

In view of the current widespread interest in the procedure of stellate ganglion block as a therapeutic procedure in cerebrovascular accidents, it is thought that the following case may be of interest.

Mr. G. J., a machinist, aged 56, awoke Feb. 1, 1951 and discovered he had great difficulty in reading. He could see the letters but could not follow them across a line to read even a short word. He had a history of three coronary occlusions during the preceding four years and had had an occlusion of the central retinal vein of the right eye with hemorrhagic glaucoma five years previously. The latter condition had been treated with diathermy to the globe, and he had retained a good field of vision, although the central acuity was reduced to 4/200.

The night before his present difficulty began, he had been reading for about an hour and had experienced a moderately severe pain in the left (normal) eye, which subsided when he stopped reading and went to bed. The next morning he was aware of nothing unusual when he awoke, but when he went to work he noticed difficulty in reading his calipers and gages. It was then that he picked up a newspaper and detected the difficulty described above. He continued on his job as a supervisor and hoped that the condition would clear up; but when it did not show any improvement by 3:00 p.m., he sought medical advice.

On examination he was found to have visual acuity of 20/30 in the left eye and 4/200 in the right eye. He had homonymous congruous field defects involving the entire upper right quadrant and the upper half of the lower right quadrant of both eyes. The upper field was out to 13 mm. white at 1 meter, although he could distinguish gross hand movements over the entire right field. In the lower half there was a relative defect which was demonstrated with 5 and 10 mm. white test objects at 1 meter, but in which he could barely distinguish the 13 mm. white object at 1 meter. The macula was "split," and above the midline the 13 mm. white was not discerned. There were no other neurological signs or symptoms, and the only other significant ocular findings were undercorrected hypermetropia and presbyopia, macular degeneration of the right eye and scarring in the temporal retina of the right eye, which had received the diathermy five years previously.

With a tentative diagnosis of probable cerebral thrombosis, the patient was referred to the anesthesia department of the Beverly Hospital, where Dr. Russell J. Rowell performed a procaine block of the stellate ganglion on the left. A pronounced Horner syndrome developed and lasted about three hours. One hour after the block was done, a check of the field showed complete clearing of the lower half of the right hemianoptic field and partial clearing of the upper field.

Another block was done the next day, and slight additional clearing was noted; but when a third block failed to produce further significant clearing on the third day, this procedure was discontinued and the patient was given a mild vasodilator (sodium nitrite, 1 grain, 0.065 Gm.) three times a day, and was advised to discontinue the use of tobacco.

During the following month, the field defect has cleared entirely except for a very small area between the 5 and 10 degree circles, and this can be demonstrated only with a 1 mm. white test object at 1 meter. It is anticipated that this will eventually clear completely.

Whether the stellate block can be given credit for all the improvement in this case is open to question. However, it seems reasonable to credit it with the dramatic improvement which took place within one hour following the initial block. The procedure certainly merits further use and study in the treatment of vascular thromboses and should be borne in mind by ophthalmologists for treatment in this type of case when seen early.

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Annual Review

DISEASES OF THE RETINA

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CONGENITAL ABNORMALITIES

During the past 10 years ophthalmologists have altered the point of view of physicians toward minor disorders of gestation by demonstrating that rubella and Toxoplasma may produce severe structural defects in the fetus. Further studies on children who were affected by maternal rubella infections during the first trimester of pregnancy (in the Australian epidemic of 1940 to 1943) have revealed a high percentage of retinal lesions. Hamilton and associates [1] studied the children in the Tasmanian Institution for the Blind, Deaf and Dumb and found that of the 29 children who were deaf from maternal rubella infections, 13 had retinitis. Morlet [2] examined 60 "rubella children" in Western Australia and found that 36 of them had chorioretinal lesions. The fundus changes were divided into three types: (1) gross and general pigmentary changes; (2) fine, pepper-like pigmentary changes mainly in the periphery, and (3) waxy, disklike lesions with no obvious pigmentary changes. None of the children in Morlet's study who were so affected showed loss of central visual acuity attributable to the retinal lesions.

Franceschetti and Bock [3] reported megalopapilla as a new congenital abnormality. A man aged 25 with a slightly hypermetropic refractive error had disks

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1. Hamilton, J. B.; Phillips, F.; Palfreyman, C. R., and Waterworth, D. H.: Rubella Retinitis in Tasmania, Tr. Ophth. Soc. Australia **8**:114, 1948.

2. Morlet, C.: Rubella Retinitis in Western Australia, Tr. Ophth. Soc. Australia **9**:212, 1949.

3. Franceschetti, A., and Bock, R. H.: Megalopapilla: A New Congenital Anomaly, Am. J. Ophth. **33**:227, 1950.

more than twice the average size. All other findings were essentially normal. A detailed description of the techniques and calculations used in determining the size of the disks is given. Francois [4] cites the case of a 2½ year old girl with a peculiar prepapillary cyst which was thought to have developed from remnants of the hyaloid arteries. Periodic observations of the fundus for six years revealed the occurrence of hemorrhages in the macular area produced by mechanical irritation brought about by movement and friction of the cyst.

EXPERIMENTAL CONGENITAL ABNORMALITIES

Ocular lesions have been produced in experimental animals by interfering with the development of the fetus. Jesberg [5] injected nitrogen mustard (methyl-bis [2-chloroethyl] amine hydrochloride) into fertile chicken eggs from zero to 96 hours after incubation. The embryos, which survived for seven to nine days, were examined histologically. In a significant number of eggs receiving injections prior to 30 hours of incubation the embryos showed microphthalmos and defective closure of the choroidal fissure. Wilson and Karr [6] irradiated the surgically exposed uterus of pregnant rats on either the ninth or the tenth day after ovulation. The embryos were removed three or four days later. Exposure to 200 r (x-rays) on the ninth day usually resulted in the death of all embryos, whereas on the tenth day a dose of 400 r was required to obtain a similar lethal effect. Sublethal doses at either age caused specific malformations in the survivors, but it required up to four times as much radiation on the tenth day as it did on the ninth day to produce lesions. In both instances the eye was the commonest site of malformation (anophthalmos and microphthalmos). The heart, urinary tract and brain were occasionally malformed.

RETROLENTAL FIBROPLASIA AND RETROLENTAL MEMBRANES

One of the most interesting retinal lesions to be studied in the past few years is retrolental fibroplasia. It is the most frequent cause of blindness in children today. Attention was first called to this disease by Terry [7] in 1942, when he described the appearance of the fully developed condition and pointed out the relation of the disease to prematurity.

In the early literature that followed, there was considerable difference of opinion as to the nature and origin of the membranes behind the lens. Terry pointed out that the condition developed after birth and suggested that the basis of this disease lay in the development of embryonic connective tissue in the meshwork of a persistent tunica vasculosa lentis. Reese and Payne [8] suggested that the

4. Francois, J. A.: Pre-Papillary Cyst Developed from Remnant of the Hyaloid Artery, Brit. J. Ophth. **34**:365, 1950.

5. Jesberg, D. O.: Experimentally Produced Ocular Abnormalities in Chick Embryos; abstracted, Anat. Rec. **106**:305, 1950.

6. Wilson, J. G., and Karr, J. W.: Difference in the Effects of X-Irradiation in Rat Embryos of Different Ages, abstract, Anat. Rec, **106**:259, 1950.

7. Terry, T. L.: Extreme Prematurity and Fibroblastic Overgrowth of Persistent Vascular Sheath Behind Each Crystalline Lens: Preliminary Report, Am. J. Ophth. **25**:203, 1942; Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Infants Born Prematurely: III. Studies in Development and Regression of Hyaloid Artery and Tunica Vasculosa Lentis, ibid. **25**:1409, 1942.

8. Reese, A. B., and Payne, F.: Persistence and Hyperplasia of the Primary Vitreous: Tunica Vasculosa Lentis or Retrolental Fibroplasia, Am. J. Ophth. **29**:1, 1946.

retrolental membrane represented hyperplastic remnants of the primary vitreous. Krause [9] thought that the disease was part of a syndrome and that the essential lesion was a prenatal abnormality of the cerebral and neuroretinal ectoderm. Owens and Owens [10] were the first to study the ophthalmoscopic appearance of retrolental fibroplasia from the time of onset to the end stage of the disease in premature infants. From their observations, they concluded that the primary lesion occurred in the peripheral retinal blood vessels and that the disease was in no way connected with the persistence of the hyaloid system or primary vitreous.

The earlier differences of opinion as to the nature of the retrolental membranes in children have been greatly clarified by a number of workers. It is now agreed that there are several types of lesions which may produce a retrolental membrane in infants. These are (1) retrolental fibroplasia; (2) encephalo-ophthalmic dysplasia, or retinal dysplasia; (3) persistence of the tunica vasculosis lentis, or hyperplastic vitreous, and (4) pseudoglioma.

Retrolental fibroplasia is by far the most important of these conditions because of its tremendous increase in incidence. This is a disease of premature babies, in which the first clinical manifestations appear from some time after birth up to the fourth month of postnatal life. In the cases studied by Owens and Owens the eyes of the premature infants in which retrolental fibroplasia subsequently developed did not differ when first examined a few days after birth from the eyes of the premature infants that remained normal. The earliest detectable change was a dilatation of the retinal vessels and an increase in the tortuosity of the retinal arteries. Localized or generalized swelling of the retina soon followed, and the retina developed a grayish green color. Often the course of the retinal vessels could not be traced in areas of the greatest edema. The vitreous became cloudy, and proliferation of fibrous bands extended forward from the elevated retina into the vitreous. A retrolental membrane was formed by fusion of the vitreous bands and peripheral folds of the swollen elevated retina. These workers were able to follow the complete regression of the tunica vasculosa lentis and the hyaloid artery in a number of instances, but in the 18 cases of retrolental fibroplasia in which they observed the disease develop the two conditions were entirely unrelated.

The clinical appearance at the onset of the disease as just described has been confirmed by Gilger,[11] Falls,[12] LaMotte and Tyner,[13] Holm,[14] Arruga [15] and

9. Krause, A. C.: Congenital Encephalo-Ophthalmic Dysplasia, Arch. Ophth. **36**:387 (Oct.) 1946.

10. Owens, W. C., and Owens, E. U.: Retrolental Fibroplasia in Premature Infants, Am. J. Ophth. **32**:1, 1949.

11. Gilger, A. P.: Retrolental Fibroplasia in Prematurely Born Children, Am. J. Ophth. **32**:917, 1949.

12. Falls, H., in discussion on Reese, A. B.: Persistence and Hyperplasia of Primary Vitreous: Retrolental Fibroplasia—Two Entities, Arch. Ophth. **41**:527 (May) 1949.

13. LaMotte, W. O., Jr., and Tyner, G. S.: Observations on Retrolental Fibroplasia, Arch. Ophth. **44**:620 (Oct.) 1950.

14. Holm, E.: Retinopathia Praematurorum (Retrolental Fibroplasia), Acta ophth. **27**:623, 1949.

15. Arruga, H.: Fibroplasia, retrolental, Arch. Soc. oftal. hispano-am. **10**:468, 1950.

Lelong and associates.[16] Gilger mentions the early appearance of retinal and vitreous hemorrhages. Falls noted the lesion in a 2½ pound (1,134 Gm.) baby three days after birth.

Owens and Owens have stated that the active phase of the disease usually stops between the fourth and the fifth month of the infant's life and the changes that occur after this time are due to contraction of previously formed fibrous tissue. If the membrane behind the lens is complete, all vision is lost. Microphthalmos results from an arrest in the growth of the premature infant's eyes. The anterior chamber becomes shallow; posterior synechias form, and the iris develops a grayish, atrophic appearance. With the ophthalmoscope broad ciliary processes can be seen extending into the membrane at its periphery, and numerous vessels are present on the surface of the membrane. In some cases there is further shallowing of the anterior chamber with extension forward of the iris and lens in a domelike fashion. Secondary glaucoma may result. Occasionally the disease is not so extensive, and when it subsides only a partial membrane or band resembling a retinal fold is found. These eyes are often myopic and may show disseminated areas of irregular pigmentation.

The prognosis for visual acuity is extremely poor, but King[17] found that of 210 children whom he was able to test, 23 had 20/200 vision or better in one eye. Babies of higher birth weights were found to have the best chance of retaining some vision. Congenital abnormalities other than the ocular defects did not occur more frequently in patients with retrolental fibroplasia than in babies of similar birth weight, nor did the children show a higher incidence of real mental retardation than the average group of premature children (King).

The other conditions which may produce a retrolental membrane, such as encephalo-ophthalmic dysplasia, or retinal dysplasia, have not increased appreciably in incidence during the past 10 to 15 years.

Encephalo-ophthalmic dysplasia of Krause,[9] or the retinal dysplasia of Reese,[18] is not related to prematurity and is always bilateral. In some cases true microphthalmos occurs, the eyes being so small that they are difficult to find in the orbits. There are usually accompanying abnormalities of the brain, heart, vascular system or skeleton, one or a number of which often cause an early death. Reese found 18 cases of this condition reported in the literature and reports an additional eight cases of his own. On pathological study, he found that the most conspicuous feature was the malformation of the retinal elements with the formation of true rosettes. The retina was detached in part or wholly and lay in folds against, and enmeshed in, vascular connective tissue just behind the lens. This fibrous tissue was viewed as a persistence of the primary vitreous. The retinal malformation was associated with other ocular abnormalities, such as coloboma of the uvea or optic nerve and retrobulbar cyst.

Persistence of the tunica vasculosa lentis, or hyperplastic primary vitreous, occurs in full-term infants and is usually unilateral. Minute remnants of the hyaloid system are seen frequently, but a fully developed retrolental membrane as a result of this lesion is rare.

16. Lelong, M.; Velter, E.; Desivignes, P.; Rossier, A., and Baron, J. D.: Deux cas de fibroplasia retro-lentale, Bull. Soc. opht. France, p. 73, March 1950.

17. King, M. J.: Retrolental Fibroplasia: A Clinical Study of 238 Cases, Arch. Ophth. 43:694 (April) 1950.

18. Reese, A. B., and Blodi, F. C.: Retinal Dysplasia, Am. J. Ophth. 33:23, 1950.

Pseudoglioma is a clinically descriptive term that has been used in the past to refer to retrolental membrane of unknown origin. It may result from a massive vitreous hemorrhage or intrauterine uveitis. This condition may be unilateral or bilateral and is not necessarily associated with prematurity (Wolff [19] and Heath [20]).

Retinoblastoma may also produce a whitish mass behind the lens, but this condition is not included in the group of benign retrolental membranes.

A number of studies have been made on the pathological appearance of retrolental fibroplasia (Reese,[21] Klien,[22] Wolff [19] and Heath [20]). Most of the reports have been based on studies of the late stages of the disease, in which the retina is completely detached and is enmeshed in a fibrous mass behind the lens. In two reports, however, the specimens were obtained in the early stages of the condition. In one of these, Reese [21] found a thin layer or localized clumps of small blood vessels with relatively little supporting tissue over the entire surface of the retina. These vessels lay along the surface of the internal limiting membrane or appeared elsewhere in the nerve fiber layer. He concluded that the pathological picture represented the persistence of hyperplastic primary vitreous on the surface of the retina. In the second, Heath [20] reports the examination of an eye removed 18 hours after birth from an infant that weighed 3½ pounds (1,534 Gm.). This eye showed the presence of a pupillary membrane, postlental hyaloid vessels, a fold in the retina near the disk and a persistent hyaloid artery. There was a hemorrhage beneath the retina at its anterior attachment and edema and hemorrhage in its peripheral portion. In places the internal limiting membrane was broken, and from these areas new-formed connective tissue migrated to the anterior surface of the retina. Blood cells were also noted in the vitreous. Heath concluded that the primary site of the disease was in the vessels and retina.

The etiology of retrolental fibroplasia is not known. It is suggested by Reese [21] and Klien [22] that the disease is antenatal in origin. They base their opinion on histological studies of the disease which they believe demonstrate that the primary lesion represents a persistence of the primary vitreous in the periphery of the fundus. Owens and Owens [23] and Kinsey and Zacharias [24] think that the condition is postnatal in origin. Their conclusion is the result of clinical observations on the development of the disease.

Excessive exposure of the eyes of premature infants to light has been suggested as a cause of retrolental fibroplasia. Hepner, Krause and Davis,[25] in an interesting

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19. Wolff, E.: Pathologic Aspects of Retrolental Fibroplasia, Am. J. Ophth. **33**:1768, 1950.

20. Heath, P.: Retrolental Fibroplasia as a Syndrome: Pathogenesis and Classifications, Arch. Ophth. **44**:245 (Aug.) 1950.

21. Reese, A. B.: Persistence and Hyperplasia of Primary Vitreous: Retrolental Fibroplasia —2 Entities, Arch. Ophth. **41**:527 (May) 1949.

22. Klien, B. A.: Histopathologic Aspects of Retrolental Fibroplasia, Arch. Ophth. **41**:553, (May) 1949.

23. Owens, W. C., and Owens, E. U.: Retrolental Fibroplasia in Premature Infants: II. Studies on Prophylaxis of the Disease; the Use of Alpha Tocopherol Acetate, Am. J. Ophth. **32**:1631, 1949.

24. Kinsey, V. E., and Zacharias, L.: Retrolental Fibroplasia: Incidence in Different Localities in Recent Years and a Correlation of the Incidence with Treatment Given the Infants, J. A. M. A. **139**:572 (Feb. 26) 1949.

25. Hepner, W. R.; Krause, A. C., and Davis, M. E.: Retrolental Fibroplasia and Light, Pediatrics **3**:824, 1949.

study, kept covered the eyes of five infants who weighed less than 3 pounds (1,307 Gm.) at birth until the babies attained a weight of 6.6 pounds (2,994 Gm.). In four of these five infants retrolental fibroplasia developed.

Kinsey and Zacharias,[24] in an extensive study, concluded there was no correlation between retrolental fibroplasia and the parity or age of the mother, Rh type, type of delivery, analgesia and anesthesia used, cause of prematurity, single or multiple birth, sex, increase in the survival rate of premature infants or congenital abnormalities other than the ocular defect. They did find, however, that there was a positive correlation between the rise in incidence of the disease and the use of two supplements of water-soluble vitamins and iron. Hepner, Krause and Nardin [26] have confirmed these findings.

Owens and Owens [25] believe that retrolental fibroplasia is due to a vitamin E deficiency. They observed that one of the main physiological differences between premature and full term infants is the defective fat metabolism of premature infants. Because of this defect, the diet given premature infants in most hospitals is low in fat and high in protein. Since low fat diets contain few fat-soluble vitamins, vitamins A, D and K are given in supplementary amounts. Fat-soluble vitamin E is not generally supplemented, though it has recently been shown in experimental animals that the need for vitamin E is increased when vitamin A or unsaturated fats are administered. It is also known that ferric salts destroy vitamin E. Large amounts of vitamin A in the form of neutral fish liver oils, which contain unsaturated fats, or of vitamin A in water-soluble preparations and ferric salts are given premature infants. These supplements produce a further depletion of vitamin E in these babies. Because of these observations, it occurred to Owens and Owens that retrolental fibroplasia might be due to a vitamin E deficiency. In order to test this hypothesis, infants weighing less than 3 pounds at birth were given 150 mg. of *dl*-alpha tocopherol acetate daily. Of 23 premature infants so treated, only one baby, or 4.4 per cent, had the disease, whereas of 78 babies who did not receive the supplement, 17, or 21.8 per cent, were affected. It is interesting that the one infant in the group with supplemented vitamin intake in whom retrolental fibroplasia developed showed progression of the disease, even though the serum tocopherol level was adequate from the time the first retinal change appeared. These results are said to be encouraging, and the suggestion is made that further data be accumulated before a critical evaluation of the role of vitamin E in the disease can be made.

Reports from other workers have thrown doubt on the efficiency of vitamin E supplements in preventing retrolental fibroplasia. In three of 17 premature infants described by LaMotte and Tyner [13] the disease developed notwithstanding supplementation of vitamin E from shortly after birth. These three babies had adequate tocopherol serum levels. Reese [27] states that vitamin E is not effective in preventing or arresting the disease. He found, however, that the pituitary adrenocorticotropic hormone (ACTH) was of value in arresting the early stages of retrolental fibroplasia. Woods [28] reports the use of this hormone in two infants. It did not influence the progress of the lesion.

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26. Hepner, W. R.; Krause, A. C., and Nardin, H. E.: Retrolental Fibroplasia: II. Encephalo-Ophthalmic Dysplasia; Study of 66 Cases, Pediatrics **5**:771, 1950.

27. Reese, A. B.: Retrolental Fibroplasia, Arch. Ophth. **44**:754 (Nov.) 1950.

28. Woods, A. C.: ACTH and Cortisone in Ocular Disease, Am. J. Ophth. **33**:1325, 1950.

It is agreed by all workers that the incidence of retrolental fibroplasia has increased tremendously in the past 10 to 15 years. It is interesting that the number of cases varies appreciably from city to city, from hospital to hospital in the same city and from year to year in the same hospital. The most dramatic illustration of this is the report of Hepner, Krause and Nardin [26] from the Chicago Lying-in Hospital, in which the percentage of retrolental fibroplasia in premature infants weighing less than 3 pounds at birth varied from 6.8 per cent, between 1937 and 1945, to 30.4 per cent, between 1946 and 1948. Kinsey [29] states that in cities where the incidence is relatively low the disease seems to be confined to infants of less than 3 pounds in weight at birth, but where it is higher the disease is also present in heavier premature infants. Lowenfeld [30] reports that of 843 blind preschool children who were registered in 1950 in New York, New Jersey, California and Connecticut, 42 per cent were blind from retrolental fibroplasia. Heretofore most of the studies on retrolental fibroplasia have been done in this country. However, during the past year cases have been reported from England, Denmark,[14] France [16] and Spain. Crosse found that 0.8 per cent of babies weighing under 4 pounds at birth and 4.2 per cent of those weighing under 3 pounds, born in Birmingham, England, had the disease. Moffatt [32] found that of 119 children in homes for preschool blind children in England, approximately 10 per cent had retrolental fibroplasia.

RETINAL TUMORS

Rados [33] published a monograph on hemangioblastoma of the retina in which he reported histological examination of such lesions in two eyes that were removed for absolute glaucoma. One patient was a girl aged 16 with absolute glaucoma of one eye and a hemangioblastoma in the upper nasal portion of the fundus of the second eye. The other patient was a man aged 28 whose left eye had been removed for absolute glaucoma. The diagnosis in this case was not suspected until routine pathological examination disclosed the true nature of the underlying condition. Pathological examination revealed that the tumor in each case was a true intraretinal capillary hemangioblastoma. In the first case, the subretinal transudate was extremely rich in cholesterol crystals. In the second, the number of crystals was negligible, but the transudate exhibited large numbers of swollen, desquamated and proliferating pigment epithelium derivatives, corresponding to ghost cells. In the second case the hyperplastic connective tissue elements between the capillary loops were extremely prominent. In one case the tumor was located near the disk, and in the other it was in the upper temporal part of the retina.

This monograph does not lend itself to abstracting, but it is the most complete and up-to-date article on the subject, an excellent reference for future studies on the disease. A comprehensive review of previous reports on the clinical and patho-

29. Kinsey, V. E.: Present Status of Retrolental Fibroplasia, Arch. Ophth. **44**:749 (Nov.) 1950.

30. Lowenfeld, B.: Meeting the Needs of Visually Handicapped Preschool Children, Sight-Saving Rev. **20**:145, 1950.

31. Footnote deleted.

32. Moffatt, P.: Retrolental Fibroplasia (Clinical Aspects of Retrolental Fibroplasia), Proc. Roy. Soc. Med. **43**:223, 1950.

33. Rados, A.: Hemangioblastoma of the Retina (von Hippel-Lindau Disease), Arch. Ophth. **43**:43 (Jan.) and 265 (Feb.) 1950.

logical appearance of the lesion is given. The coexistence of tumors in the retina and brain, the mode of inheritance, the differential diagnosis of angiomatosis retinae and retinitis exudativa (Coats's disease) and the differential diagnosis of angioma and hemangioblastoma of the retina are discussed.

The case of a man aged 24 whose eye was removed because of a suspected tumor is reported by Michaelson and Hill.[34] The left eye was normal. In the right eye there was a large globular detachment of the retina in the lower nasal quadrant with several smaller detachments above. A cerebellar tumor was subsequently removed and was diagnosed as a hemangioblastoma. Histological examination of the eye revealed multiple nodules in the retina, which consisted of a fibrocellular matrix with new vessels of varying size and a nest of endothelial cells. Some of these lesions filled the entire thickness of the retina. In places there was hyaline degeneration of the nodules. Cystic, pigmentary and other forms of degeneration occurred in the retina and pigment epithelium. The authors thought that the tumor cells were not derived from the large, mature retinal vessels but probably originated from the capillary endothelium or an anlage of such endothelium.

Frandsen[35] reports the case of a woman aged 33 who had marked cyanosis from an arteriovenous aneurysm of the lung. The patient gave a history of progressive deterioration of vision in the left eye over a period of three years. Examination revealed a 2 mm. proptosis of the left eye. The retinal vessels in the right eye were congested and cyanotic. In the fundus of the left eye there was 3 D. of papilledema with variform tortuous vessels. The pulmonary arteriovenous aneurysm was repaired surgically. The proptosis of the left eye subsided, and the edema of the left disk was reduced to 1 D. of elevation. The author believes that the unusual appearance of the left fundus was caused by a hemangioma in the optic disk.

Reese[36] studied inheritance in relation to retinoblastoma from two points of view: First, when a retinoblastoma has occurred in one child of healthy parents, what is the likelihood that further siblings will be affected? Second, is it advisable for the adult survivor of retinoblastoma to have children? In answer to the first question, he collected from the literature and from his own patients 150 cases of retinoblastoma in children, who had a total of 378 siblings. Among the siblings there was only one case of retinoblastoma, making the incidence less than 2.9 in 1,000. Because of this, he does not hesitate to advise healthy parents who have had one child with retinoblastoma to have more children. In answer to the second question, in his series of 184 cases of retinoblastoma, only five of the survivors had children. Of the eight children, seven had bilateral retinoblastomas. For this reason, he strongly advises survivors of retinoblastoma not to bear progeny.

Merriam[37] studied the autopsy reports on 17 patients who had died of retinoblastoma. In 16 cases there was some form of intracranial metastases, but in only 8 was the disease confined to the head or spinal cord. The lymph nodes were involved in 8 cases, the skull bones in 9, distant bones in 9 and viscera in 8. In 15 cases the orbit or optic nerve was involved. The cause of death was thought to be

34. Michaelson, I. C., and Hill, J.: Von Hippel-Lindau Disease: Clinical and Pathological Report of a Case, Brit. J. Ophth. **33**:657, 1949.

35. Frandsen, A. D.: A Case of Hemangioma Retinae, Acta ophth. **28**:97,1950.

36. Reese, A. B.: Heredity and Retinoblastoma, Arch. Ophth. **42**:119 (Aug.) 1949.

37. Merriam, G. R., Jr.: Retinoblastoma: Analysis of 17 Autopsies, Arch. Ophth. **44**:71 (July) 1950.

intracranial involvement in 9 cases, generalized carcinomatosis in 7 cases and invasion of the nose and mouth, making respiration and swallowing impossible, in 1 case. The most important aspect of this analysis is the finding that retinoblastoma is not the purely local and cranial disease it is often considered. It is, rather, a highly malignant and widely disseminated neoplasm.

PRIMARY CHORIORETINAL ABERRATIONS WITH NIGHT BLINDNESS

The present state of our knowledge of primary chorioretinal aberrations with night blindness was summarized in a symposium at the Fifty-Fourth Annual Session of the American Academy of Ophthalmology and Otolaryngology in 1949. Leinfelder [38] pointed out that a classification of these lesions was necessarily arbitrary, for the precise histopathology of many of these conditions is not known. The clinical characteristics of the diseases were, therefore, utilized in formulating the various divisions.

The numerous aberrations were divided into groups and subgroups, most readily presented in the following outline:

I. Congenital stationary night blindness
   - A. Without ophthalmoscopic abnormality
   - B. Without ophthalmoscopic but with other abnormalities (myopia, amblyopia, nystagmus)
   - C. Characterized by changes in the color of the fundus (Oguchi's disease)
   - D. Characterized by white dots in the fundus (retinitis punctata albescens)

II. Delayed or progressive night blindness
   - A. Retinitis punctata albescens of the progressive type
   - B. Retinitis pigmentosa
     1. Without significant associated defects
     2. With significant associated defects, such as myopia, atypical chorioretinal changes and such systemic defects as deafness, mental deficiency, various neurological disturbances and the Laurence-Moon-Biedl syndrome
   - C. Gyrate atrophy and choroideremia (progressive atrophies of the choroid and retina)

Carroll [39] discussed the symptoms, signs and differential diagnosis of these diseases. The symptoms and signs need not be repeated, for they are well known. The reader is referred to Carroll's article for an excellent brief summary of these lesions. Several points of special interest should be mentioned, however. Retinitis pigmentosa sine pigmento is not described as a separate entity, for it usually indicates merely an early stage of retinitis pigmentosa. Sixteen cases of unilateral retinitis pigmentosa have been reported. One of the patients was under observation for 10 years and another for 6 years, without showing involvement of the second eye. Congenital night blindness without ophthalmoscopically visible abnormalities must be differentiated from vitamin A deficiency. Primary retinitis pigmentosa must be differentiated from numerous secondary degenerations. These include retinitis caused by syphilis, trauma, measles, rubella, vaccinia, scarlet fever, malaria and typhus in the patient or rubella in the patient's mother during pregnancy. Retinitis pigmentosa with macular involvement, such as is often seen in the

38. Leinfelder, P. J.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Classification, Tr. Am. Acad. Ophth. **54**:607, 1950.

39. Carroll, F. D.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Symptoms, Signs and Differential Diagnosis, Tr. Am. Acad. Ophth. **54**:609, 1950.

Laurence-Moon-Biedl syndrome, may appear similar to the lesion in amaurotic familial idiocy, but the progressive mental deterioration in the latter condition is characteristic. The early changes in gyrate atrophy and choroideremia may resemble each other ophthalmoscopically, but in gyrate atrophy the scalloped edges of the atrophic areas are characteristic. The type of inheritance is entirely different in the two conditions. Primary choroidal sclerosis is at times difficult to differentiate from choroideremia, but the former disease usually begins later in life and in some cases may be limited to the central area of the fundus.

Falls [40] presents the mode of inheritance of retinitis pigmentosa and allied diseases. He briefly summarizes the terminology used in modern genetics. He points out that the same clinical disease may present different inheritance modes in different families and, for this reason, no reliable advice as to transmission can be given to an affected person until the nature of his or her specific pedigree is carefully worked out. The mode of inheritance of congenital stationary night blindness is dominant, autosomal, recessive autosomal or sex-linked recessive. When stationary retinitis pigmentosa albescens is restricted to retinal degeneration characterized by the presence of innumerable white discrete dots scattered over the entire fundus with or without minimal pigmentary changes, the inheritance pattern is autosomal recessive. There are five modes of transmission of retinitis pigmentosa: (1) dominant autosomal, (2) recessive autosomal, (3) sex-linked recessive, (4) incomplete sex-linked dominant and (5) incomplete sex-linked recessive. The recessive autosomal is the commonest form of inherited transmission of this disease. There are two chief theories of the manner of inheritance of the Laurence-Moon-Biedl syndrome: (1) One gene, recessive autosomal, is responsible for numerous defects, and (2) the changes are produced by two or more genes. In gyrate atrophy of the choroid and retina the inherited pattern is chiefly autosomal recessive. In choroideremia the mode of transmission is in intermediate, sex-linked, X-borne gene trait in which the heterozygous, or carrier, female exhibits a specific, but atypical, picture of retinal and choroidal aberration but has no ocular symptoms. The males present a progressive choroidal abiotrophy leading to the typical and diagnostic retinal picture.

Cogan [41] gives a detailed description of the pathology of retinitis pigmentosa. He states that of the 20 cases with pathological descriptions recorded in the literature, 9 may be considered authentic. His report is based on a study of five cases, two of which have been reported previously, one by Verhoff and one by Friedenwald. There were no histological features which were pathognomonic of retinitis pigmentosa. However, the prime pathological changes consisted of disappearance of the rods, cones and outer nuclear layer and migration of the retinal pigment epithelium into the neuroepithelial layers. True fusion of the retina to the outer layers was conspicuously absent except for an occasional diaphanous strand in the far periphery of the fundus. The inner retinal layers were preserved even in the late stages of the disease. Cogan thinks that the pigmentation of the retina was a secondary process, probably conditioned by the contact of the sievelike external limiting membrane with the pigment epithelium, causing subsequent migration of

40. Falls, H. F.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Genetics, Tr. Am. Acad. Ophth. **54**:617, 1950.

41. Cogan, D. G.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Pathology, Tr. Am. Acad. Ophth. **54**:629, 1950.

epithelial cells into the retina. Once in the retina, the pigment cells had a preference for the perivascular regions but also formed nests of cells independent of the vessels. These nests were probably the counterpart of the bone corpuscles seen on ophthalmoscopic examination. The retinal arteries showed moderate periarterial thickening and hyalinization of the walls, but to a less degree than would be expected from the apparent constriction seen with the ophthalmoscope. It was not apparent why the retinal arteries should be narrowed, since the layers of retina supplied by these arteries were well preserved. The optic nerve was essentially normal in four of the five eyes examined. The fifth eye had absolute glaucoma. Gliosis of the optic nerve was also an inconspicuous feature. There was little found on histological study to account for the pallor of the disk, which has so often been described ophthalmoscopically. Bruch's membrane and the choriocapillaris showed no significant abnormalities. There was some sclerosis of the choroidal arteries but not sufficient to account for the retinal changes.

It is pointed out that a number of lesions, such as long-standing dislocation of the lens into the vitreous, trauma in childhood, corneal ulcers in childhood with perforation and secondary glaucoma, syphilitic retinitis and occlusion of the posterior ciliary arteries, may produce lesions similar to retinitis pigmentosa. They may be differentiated from the specific disease, however, by the more extensive destruction of the inner layers of the retina, the denser pigmentation in the retina, the disappearance of the pigment epithelium and true chorioretinal adhesions. The macular changes in some of the hereditary dystrophies (cerebral macular degeneration, Vogt-Spielmeyer disease) may be very similar to the peripheral changes seen in retinitis pigmentosa. Senile macular degeneration was also analogous, but there is greater involvement of all layers of the retina, and true chorioretinal adhesions may occur. The histological changes produced in the retina by vitamin A deficiency in experimental animals closely resembled those seen in retinitis pigmentosa in man.

McCulloch [42] describes the histopathological changes in four eyes from two patients with choroideremia whom he had observed clinically. This report was not included in the symposium. The essential finding in these four eyes was atrophy of the choroid and choroidal vessels. The choroid was completely missing at the equator, but at the ora serrata and posterior pole of the globe some remnants of tissue and a few sclerotic vessels remained. The rods, cones and the outer nuclear layer for the most part were missing, and in places the disorganized retina was fused with the remains of the choroid. The bipolar cells, ganglion cells and nerve fiber layer remained intact for the most part in three eyes. In one eye glaucoma had attenuated these layers. In the macular areas some pigment epithelium remained, and a few rods and cones could be seen with their nuclei. This work indicates that the primary lesion in choroideremia is a destruction of the choroidal vessels.

During the symposium, Fralick [43] discussed the treatment of chorioretinal aberrations. He listed many of the forms of treatment, such as administration of vasodilator drugs, surgical vasodilation, use of physical agents, drugs to increase general body tone and hormones, vitamin therapy and tissue therapy, which have been used to arrest the progress of the disease. His conclusion was that up to the

42. McCulloch, J. C.: The Pathologic Findings in 2 Cases of Choroideremia, Tr. Am. Acad. Ophth. **54**:565, 1950.

43. Fralick, F. B.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Treatment and Conclusions, Tr. Am. Acad. Ophth. **54**:662, 1950.

present time all of these agents have failed to arrest the progress of the diseases. It was pointed out that patients with congenital stationary night blindness can be expected to retain their vision throughout life unless secondary complications occur. In the group of delayed or progressive primary chorioretinal aberrations it was much more difficult to prognosticate the final visual outcome. The prognosis for cataract surgery was surprisingly good in patients with retinitis pigmentosa when vision was as poor as 20/200. The operation offered no more complications than did cataract extraction in an ordinary patient.

Duke-Elder [44] concluded the symposium by questioning the advisability of grouping primary choroidal aberrations and primary retinal aberrations under the same heading.

A number of reports [45] have appeared in the past year on the management of retinitis pigmentosa with vitamins and Filatov's tissue therapy. Most of these reports indicate that there has been no lasting improvement from this type of treatment.

Several interesting cases of retinitis pigmentosa have been reported. Hegner [46] observed an 18 year old girl who had a marked constriction of the visual field on the second, third and fourth days after the beginning of menstruation. During the intramenstruum her visual fields were almost normal in size. Three cases of unilateral retinitis pigmentosa are described.[47] In one of these the patient was observed for 10 years without the development of symptoms in the other eye. Bassen and Kornzweig [48] cited the case of an 18 year old girl with atypical retinitis pigmentosa who had involvement of the macula. Neurological examination revealed diffuse disease of the central nervous system (Friedreich's ataxia). The red blood cells had a peculiar crenated appearance, due to the presence of pseudopods or protoplasmic projections, varying in size and shape. A similar blood picture and beginning pigmentary degeneration were observed in a younger brother.

The association of deafness with the Laurence-Moon-Biedl syndrome is discussed by Burn.[49] He reviews the cases of this syndrome which have been reported since 1937 and analyzes all the case reports published since 1864 in which deafness was recorded in connection with the disease. Two new families with the Laurence-

44. Duke-Elder, S.: Symposium: Primary Chorioretinal Aberrations with Night Blindness; Discussion, Tr. Am. Acad. Ophth. **54**:666, 1950.

45. Saltzman, S. L., and Haig, C.: Treatment of Retinitis Pigmentosa with Cod Liver Oil Injections and Placental Implantation, Arch. Ophth. **43**:419 (March) 1950. Klenka, L.: Degeneratio retinae pigmentosa, Československ. ofth. **6**:107, 1950. Tcherkes, L. A.; Averbach, D. M., and Iakovleva, S. P.: Use of Vitamin A in Retinitis Pigmentosa, Vestnik. oftal. **29**:33, 1950. Domínguez, D. D.: Empleo de la vitamina E en las degeneraciones retinianas, Medicina, Madrid **18**:34, 1950. Symposium: Reservée à la therapeutique tissulaire, Bull. Soc. opht. France, p. 299, May 1950.

46. Hegner, H.: Über Retinitis pigmentosa und innere Sekretion, Ophthalmologica **118**: 637, 1949.

47. Gordon, D. M.: Unilateral Retinitis Pigmentosa: Report of a Case, Am. J. Ophth. **32**:1350, 1949. Hurwitz, P.: Unilateral Retinitis Pigmentosa with Aniseikonia, Eye, Ear, Nose & Throat Month. **29**:259, 1950. Maeder, G., and Muller, P.: Rétinite pigmentaire unilatérale, Ann. ocul. **183**:771, 1950.

48. Bassen, F. A., and Kornzweig, A. L.: Malformation of the Erythrocytes in a Case of Atypical Retinitis Pigmentosa, Blood **5**:381, 1950.

49. Burn, R. A.: Deafness and the Laurence-Moon-Biedl Syndrome, Brit. J. Ophth. **34**:65, 1950.

Moon-Biedl syndrome are reported. In one family, the offspring of a first-cousin marriage consisted of two females with the complete syndrome, one female who died young but was reputed to have had polydactyly, two male deaf-mutes, two normal females and two normal males. The second family, offspring of unrelated parents, consisted of two affected sibs, a female who showed the complete syndrome and a male who lacked only polydactyly. Burn pointed out that deafness was present in 18 of 611 members of affected sibships, an incidence of 2.94 per cent or nearly 60 times that which occurs in the general population.

Gartner and Schlossman [50] described eight cases of retinitis pigmentosa associated with glaucoma. In three of the cases histological examination was made. Pigmentation of the chamber angle was observed both gonioscopically and pathologically but was not sufficient in amount to produce mechanical blocking of the angle.

Brand [51] reports the case of an 8 year old girl who had the Laurence-Moon-Biedl syndrome. Her fundus changes were compatible with retinitis pigmentosa, but in addition she had degenerated areas in the fundus similar to those seen in gyrate atrophy.

SECONDARY PIGMENTARY DEGENERATIONS OF THE RETINA

Several cases of secondary pigmentary degeneration of the retina have been noted. A girl 12 years of age received an unknown dose of quinine,[52] after which she had a marked loss of vision. Her central visual acuity was reduced; her visual field was restricted to 5 degrees, and bone corpuscle pigmentation developed in the periphery of the fundus. A white woman aged 27 with unilateral pigmentary degeneration of the retina was observed who had a semitranslucent, greenish, smooth, pear-shaped cyst of undetermined nature in the lower portion of the vitreous.[53] A man aged 41 had marked loss of vision on the tenth day of an attack of encephalomyelitis.[54] His visual fields were constricted to 10 degrees over a period of three years, and four years after the onset of his illness pigmentary changes developed in both fundi.

Pillat [55] described the clinical picture of senile pigmentary degeneration of the retina. This consisted of a girdle-shaped pigmentary disturbance in the equatorial zone of the fundus with slight concentric constriction of the visual fields but no symptoms of day blindness. He theorized that the senile vascular changes in the choroid which produced this lesion occur first in the equatorial zone because this area is supplied by the terminal branches of the anterior posterior choroidal arteries.

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50. Gartner, S., and Schlossman, A.: Retinitis Pigmentosa Associated with Glaucoma, Am. J. Ophth. **32**:1337, 1949.

51. Brand, I.: Eine seltene Netzhautveränderung beim Laurence-Beidlschen Syndrom, Klin. Monatsbl. Augenh. **116**:338, 1950.

52. Dekking, H. M.: Pigmentary Degeneration of the Retina After Quinine Intoxication, Ophthalmologica **118**:743, 1949.

53. Wagenaar, J. W.: A Case of Unilateral Symptomatic Retinitis Pigmentosa, Ophthalmologica **118**:1031, 1949.

54. Maeder, G.: Rétinite pigmentaire après maladies à virus (À propos d'un cas de rétinite pigmentaire, survenu après encéphalite), Ophthalmologica **118**:746, 1949.

55. Pillat, A.: Die senile Pigmentierung der Netzhaut (senile Pigmententartung), Arch. f. Ophth. **150**:1, 1950.

MACULAR LESIONS

Sorsby, Mason and Gardener [56] describe an unusual dystrophy of the fundus in five families. The genetic nature and dominant inheritance of the lesion were shown by evidence of direct transmission over four generations. The outstanding features were a bilateral central lesion of late onset, with edema, hemorrhages and exudates in the early stages, developing into generalized choroidal atrophy. There was no night blindness antecedent to the development of the fundus lesions or during the evolution of the affection. The disease first appeared in persons in the early forties with a defect of central vision, which was intensified and spread to the periphery, though only in the severest cases did total blindness ensue. The choroidal vessels disappeared, and the terminal picture was one of extensive choroidal atrophy with pigmentation. Burn [57] reports a sixth family with the disease in which 11 of the 29 members of the family who had reached 40 years of age were affected. Four generations of this family were studied. Excellent fundus drawings of the lesions from the time of onset to their advanced stage were included in both articles.

Heredodegeneration of the macula lutea has been divided into four types: infantile, juvenile, presenile and senile, according to the age of the patient. The pattern of development with regard to time of onset, fundus picture and rate of progress is usually identical in all the affected members of the same family. Klien [58] divides the lesions into three types according to the appearance of the macula. Type 1 was characterized by inconspicuous, sharply defined, round or oval areas, which were slightly lighter red than the surrounding fundus. Type 2 showed round, yellowish areas over which there was a cystoid bulging of the internal limiting membrane. In type 3 there was a mixture of small, yellowish areas and dustlike or coarser pigment deposits. The lesions may be small and limited to the foveal region or may cover the entire macular area. A case of the fourth histological type of heredodegeneration of the macula is described. The patient, a woman aged 60, had had deterioration of vision for 15 months. Both macular areas showed a disciform, irregularly outlined, sharply defined lesion, which was surrounded by spots of pigment proliferation and a few smaller, yellowish red areas. One eye was removed because of an invading squamous cell carcinoma in the orbit. The salient features of the histopathological picture follow. 1. The first retinal neuron showed an extensive defect which was much larger than that of the second and third neurons and slightly larger than that in the pigmented epithelium. This indicated that the first neuron was the primary seat of the disease. 2. In the central portion of the lesion all layers of the retina were missing. 3. In one area there was proliferation of the pigment epithelium with calcium formation. 4. On one side of the lesion the pigment epithelium was detached from Bruch's membrane by a pale, pinkish staining, finely granular coagulum. Lesions of this type may be differentiated clinically from senile macular degeneration by the age of onset and the familial history. Histologically, the two conditions are differentiated by the absence of choroidal angiosclerosis in the hereditary form of the disease.

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56. Sorsby, A.; Mason, M. E. J., and Gardener, N.: A Fundus Dystrophy with Unusual Features, Brit. J. Ophth. **33**:67, 1949.

57. Burn, R. A.: Further Cases of a Fundus Dystrophy with Unusual Features, Brit. J. Ophth. **34**:393, 1950.

58. Klien, B. A.: The Heredodegeneration of the Macula Lutea, Am. J. Ophth. **33**:371, 1950.

Busacca [59] describes 25 cases of chorioretinitis with central retinal detachment in young adults. The lesions were studied with the Goldmann contact glass and the Haag-Streit biomicroscope. The inflammatory reaction usually began in the innermost layers of the choroid under the superior temporal vessels, destroyed the pigment layer of the retina and invaded the retina. A preretinal layer of exudate extended into the vitreous. Following this initial lesion, there was a detachment of the retina which extended to the inferior temporal vessels. In approximately half the cases which were seen early there was a complete or partial star-shaped figure in the macular region. The detachment was difficult to see with the monocular ophthalmoscope. In some cases hemorrhages occurred in the detached area. In some instances the lesions resolved, leaving very little residual damage; in others the pigment epithelium or retinal glial cells proliferated, producing a permanent scar in the macula. In 50 per cent of the cases good vision was regained after the lesion subsided. The condition in the cases described sounded like a combination of Jensen's juxtapapillary choroiditis and central serous retinopathy.

Doggart [60] describes five cases of central serous retinopathy and presents fundus drawings from these cases. In one patient edematous fluid remained in the macular area for almost four years without being absorbed. The author believes that the fluid in the macular area originated from the choriocapillaris. In a discussion of this paper, O'Day stated that he thought that the elevation of the retina was due to an actual swelling of the retinal substance.

The cases of three patients, aged 13, 14 and 26 years, with chronic progressive external ophthalmoplegia and atypical pigmentary changes in the retina, are described by Chamlin and Billet.[61] The peripheral visual fields were within normal limits. Central visual acuity was reduced to some degree in all three cases. The pigmentary changes in the retina were located both in the macula and in the peripheral area and were of the salt and pepper, rather than the bone corpuscle, type.

The case of a 13 year old girl who complained of diminution of vision at the time of her menses is described by Laub.[62] Ophthalmoscopic examination revealed yellowish, pinpoint spots in the area between the disk and the macular region. The spots disappeared in the intramenstruum and reappeared during her menses on several occasions. Eventually there developed a glial membrane which extended from the disk over the macular area and a disklike subretinal hemorrhage. Her vision was reduced to 20/400.

Gördüren [63] describes a case of congenital stationary day blindness in a man aged 31. The macular areas appeared normal. On ophthalmoscopic examination, vision was found to be 20/200 in the right eye and 20/100 in the left eye. The light threshold and dark adaptation test performed with the Birch-Hirshfeld apparatus revealed nothing pathological. In the most suitable illumination for the patient, the spectrum was composed of red, a light color similar to white, yellow and green.

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59. Busacca, A.: Sur une forme de choriorétinite avec décollement de la rétine, Arch. opht. **9**:549, 1949.

60. Doggart, J. H.: Central Serous Retinopathy, Tr. Ophth. Soc. Australia **9**:106, 1949.

61. Chamlin, M., and Billet, E.: Ophthalmoplegia and Pigmentary Degeneration of the Retina, Arch. Ophth. **43**:217 (Feb.) 1950.

62. Laub, G. R.: Progressive Retinopathy Associated with Menstruation, Am. J. Ophth. **32**:1405, 1949.

63. Gördüren, S.: Day Blindness, Brit. J. Ophth. **34**:563, 1950.

A number of investigators have described the macular changes which occurred in prisoners of war who were extremely malnourished. During the past year, three articles of note have appeared on this subject. Stoeckli-Bay and his co-workers [64] examined the fundi of 238 patients who had been interned by the Japanese for three or four years. The ages of these patients varied from 3 to 72 years. Most of these persons were seen one year after liberation. The subjective complaints consisted of day blindness, moving scotoma and difficulty in reading. Some of the patients showed a central scotoma for color, especially for yellow and blue. In one third of the patients ophthalmoscopic examination revealed absence of the foveal reflex, a granular appearance of the macular region and varying degrees of temporal pallor. Most of the patients had suffered varying degrees of malnutrition and parasitic infections, but there was no direct correlation between the macular findings and the severity of the condition. Scholtyssek [65] examined 800 prisoners of war who were fundamentally healthy but who had gone through several years of near starvation. Fifty of these patients showed sandlike spots in the macular area, and 10 of them showed degenerative changes in the posterior part of the fundus.

Obal [66] attempts to group the macular changes associated with malnutrition, snow blindness and sun blindness under the same heading. He examined 40 patients who had been heavy smokers or had suffered restricted diets, snow blindness or sun blindness. In 20 there were sandlike granular changes in the macula with central and paracentral scotomas. In five there were hyperemia and an atypical reflex of the surface of the retina. No ocular abnormality was found in 15 patients. He thinks that day blindness, night blindness and increased glare sensation are symptoms common to these various conditions.

HYPERTENSION

There has been considerable discussion in the past few years as to the value of and indications for sympathectomy in patients with hypertension. The present status of this debate is well illustrated in an article by Platt and Stanbury [67] and by the ensuing editorial responses. Platt and Stanbury believe that the majority of patients with essential hypertension could, from the point of view of sympathectomy, be divided into two classes: those whose hypertension is too mild to warrant the use of this serious operation, and those whose hypertension is too severe or who are too old or too arteriosclerotic to benefit from it. Despite this general condemnation, the authors admit that there is a small group in which sympathectomy has produced real, and apparently lasting, reduction of blood pressure. They report the results of sympathectomy in 80 cases of hypertension. Only cases were selected for operation in which the prognosis was judged to be unfavorable, usually with a resting diastolic blood pressure of 120 mm. of mercury or higher. In only 11 of the 80 cases was there a significant and lasting reduction of blood pressure. Most of the

64. Stoeckli-Bay, V.; Sicé, A.; Perret-Gentil, A., and Brückner, R.: Untersuchungen an früher internierten Holländern, Ophthalmologica **118**:775, 1949.

65. Scholtyssek, H.: Beobachtungen über tiefe Augenveränderungen nach Mangelernährung, Klin. Monatsbl. Augenh. **117**:1, 1950.

66. Obal, A.: Makulaschäden bei Inanition, Schneeblindheit und Sonnenblendung: Probleme der Ernährung der Netzhaut, Klin. Monatsbl. Augenh. **117**:28, 1950.

67. Platt, R., and Stanbury, S. W.: Sympathectomy in Hypertension, Lancet **1**:651, 1950.

patients with good results were young women under 40 years of age who had either essential hypertension or hypertension with good renal function. Twenty-three of the 80 patients subjected to operation died. Eleven of these succumbed either during or immediately after the procedure. Three died at home of cardiac failure, before the completion of their two stage operation, and nine died at intervals of one month to three years after operation.

Of particular interest to ophthalmologists is the influence of sympathectomy on hypertensive retinopathy. Twenty-four of the patients had papilledema, and in 12 of these there was complete resolution of the lesion. In three patients the papilledema persisted. Seven of the patients died immediately after the operation. This signifies the severity of this sign in patients with hypertension. No reliable postoperative report on the ocular fundi was recorded for two patients. In 10 other patients retinal exudates and hemorrhages which were present before operation disappeared completely. There was also a gratifying relief of severe headache in 23 of 33 patients with this symptom. The favorable changes in the ocular fundi and the relief of headache bore no relation to the postoperative blood pressure, nor did it seem to be accounted for on the basis of postoperative postural hypotension, for the favorable response persisted after any detectible postural hypotension had disappeared.

Adverse symptoms, such as postural hypotension, tachycardia, severe exertional tachycardia, fatigability, cold hands, intensification of Raynaud's phenomenon, exacerbations of the asthmatic state and decrease in male sexual function may follow sympathectomy. Although these postoperative sequelae may be disturbing to the patient, he usually regards the operation as worth while if it has removed his headache or improved his vision.

In an editorial reply, Wells, Welbourn, Harland and Shucksmith [68] disagree with the pessimistic view of Platt and Stanbury as to the value of sympathectomy in hypertensive disease. That the outcome in cases of hypertension not treated surgically is largely unknown is pointed out [69] as a serious defect in reports of the condition. Useful surveys have been made, but in no publication to date has the evaluation or follow-up study of a large series of cases been so complete as in those of hypertension treated surgically.

Bechgaard, Porsaa and Vogelius [70] studied the fundi of 485 hypertensive patients who had had a blood pressure of 160/100 for four to 11 years. The retinal vessels were normal in 160. Thirty patients had hemorrhages or exudates in their fundi, and 1 patient had blurred disk edges. The arteriolar diameters were normal in 50 per cent, narrowed in 34 and irregular in 27. In 63 per cent the arteriolovenous crossings were normal, and in the remaining 37 per cent the vein was found to be depressed but real compression was rare. The arterial reflex deviated from normal in 46 per cent of the patients, and "copper wire" arteries and sheathing were found in 4 per cent. When the cases were tabulated according to the classification of Wagener and Keyes, no convincing correlation between the degree of change in the retinal vessels and the condition of the patient was found.

68. Wells, C.; Welbourn, R.; Harland, J. C., and Shucksmith, H. L.: Sympathectomy in Hypertension, Lancet **1**:787, 1950.

69. Sympathectomy for Hypertension, editorial, Lancet **1**:768, 1950.

70. Bechgaard, P.; Porsaa, K., and Vogelius, H.: Ophthalmological Investigations of 500 Persons with Hypertension of Long Duration, Brit. J. Ophth. **34**:409, 1950.

Leopold, Kety and Jeffers [71] studied the relation of cerebral vascular resistance to the grade of hypertensive changes in the retina. The cerebral blood flow was measured by the nitrous oxide method of Kety and Schmidt, and the eyegrounds were graded according to the method of Wagener, Keith and Kernohan. Twenty-one hypertensive and three nonhypertensive subjects were studied. When the retinal vessels showed signs of hypertension, the cerebral vascular resistance was elevated. Although there was a definite tendency for the grade of retinopathy to increase as the cerebral vascular resistance increased, the exact extent to which the cerebral vascular resistance was elevated in a given case could not be predicted from the ophthalmoscopic findings.

Abt and Brückner [72] produced hypertension in rats by enclosing the left kidney in a tube of cellulose acetate and performing a nephrectomy on the right side eight to 12 days later. Indirect ophthalmoscopy was performed to avoid exciting the animals. The retinal arteries showed a variety of changes in caliber ranging from spasm in long stretches of the arteries, where they became threadlike, to a rosary-like appearance, caused by local spasm. The changes in the vessels were preceded by a rise in blood pressure. Retinal hemorrhages were seen in two animals. The constrictions in the vessels were thought to be due to spasm, since histological examination showed no degenerative changes in the narrowed portions of the vessels.

RETINAL VASCULAR TONE

During the past year a number of studies have been made on retinal vascular tone. Adler [73] summarizes the present status of our knowledge of ocular circulation. He points out that arterial pulsations may be of three types: (1) locomotion pulsation, (2) expansile pulsation and (3) tonic pulsation. The factors which favor locomotion, or serpentine, pulsation are (1) tortuous arteries, (2) dilated arteries, (3) pliable vessel walls, (4) large pulse pressure, (5) high systolic pressure, (6) slight peripheral resistance and (7) minimal viscosity of the blood. Expansile or collapsible pulsation can be seen in practically all normal subjects if high magnification is used. A collapsible pulse becomes visible with ordinary direct ophthalmoscopy as soon as the difference between the diastolic and the systolic pressure rises or as soon as the intraocular pressure rises above the diastolic arterial pressure. When a localized area of constriction is observed to pass down an arterial trunk, this is spoken of as tonic pulsation. Venous pulsation is due to a direct transmission of the arterial pulse through the vitreous to the veins. The vasomotor control of intraocular vessels is probably similar to that of the brain; i. e., it is maintained in a state of tonic dilatation and is little affected by neurogenic control. The blood flow is probably determined largely by the systemic blood pressure, the carbon dioxide and oxygen tension of the blood and the functional activity of various areas of the retina.

71. Leopold, I. H.; Kety, S. S.; Jeffers, W. A.; Hafkenschiel, J. H., and Shenkin, H. A.: Correlation of the Cerebrovascular Resistance and the Grade of Hypertensive Retinal Findings, Am. J. Ophth. **32**:365, 1949.

72. Abt, K., and Brückner, R.: Netzhautgefässspasmen bei artifiziell hypertonischen Ratten, Ophthalmologica **119**:17, 1950.

73. Adler, F. H.: Physiology of the Eye, St. Louis, C. V. Mosby Company, 1950, chap. 9, p. 246.

Marcussen and Wolff,[74] in a continuation of their studies on migraine, investigated the influence of carbon dioxide and oxygen on the prodromal symptoms of this condition. They mentioned that the preheadache phenomena, such as scintillating scotomas, drowsiness and thickness of speech, are the result of cerebral vascular vasoconstriction. The headache phase is due to dilatation of the arteries inside or outside the cranium. Five patients with visual disturbances due to the vasoconstrictive phase of migraine were studied. When a mixture of 10 per cent carbon dioxide and air was administered to these patients for three minutes by means of a face mask, there was transient clearing of the visual disturbances, with return of the symptoms to their former intensity within five minutes after inhalation of the gas was discontinued. When the carbon dioxide-air mixture was followed by one of 10 per cent carbon dioxide and 90 per cent oxygen, or when the carbon dioxide-oxygen mixture was used alone, the ocular symptoms cleared completely and did not return. The expected headache which accompanies vasodilatation following constriction did not occur. Huerkamp and Rittinghaus[75] studied the effect of inhalation of oxygen and carbon dioxide and the intravenous injection of epinephrine on the retinal blood vessels. The fundi were observed with indirect ophthalmoscopy, and the caliber of the blood vessels was compared with various sizes of small wires. The color of the disk was compared with Ostwald colors. One hundred and seven experiments were carried out on 26 normal males and females between the ages of 14 and 48. Respiration of almost pure oxygen for 10 to 15 minutes produced pallor of the disk, 30 per cent narrowing of the veins and 40 per cent narrowing of the arteries. The narrowing of the vessels was thought to be due to active constriction, since the blood pressure and pulse remained almost unaffected during the experiment. Mixtures of carbon dioxide and oxygen were inhaled for 10 to 20 minutes. When the amount of carbon dioxide in the inspired air was 1 per cent, there were a striking reddening of the disk and dilatation of the arteries and veins before the blood pressure and pulse rate were increased. When normal air was inhaled after this experiment, the vessels and disks returned to their normal state in five minutes. Respiration of a mixture containing two-thirds expired air for 25 minutes produced a response in the fundus similar to that seen in the carbon dioxide experiment. However, if the experiment was carried to the point of asphyxia and the veins dilated, the arteries decreased in caliber, the color of the disk was increased and the pulse rate and blood pressure rose rapidly. Intravenous injections of small doses (2 to 5 micrograms) of epinephrine led to dilatation of the retinal vessels. Injections of large doses (10 to 100 micrograms) caused a primary constriction of the vessels, followed by secondary dilatation.

Bietti and de Gaspare[76] studied the influence of inhalation of pure air at atmospheric pressure on visual field defects caused by various diseases of the eye and the central nervous system. Examinations of the visual fields were carried out

74. Marcussen, R. M., and Wolff, H. G.: Studies on Headaches: 1. Effects of Carbon Dioxide-Oxygen Mixtures Given During Preheadache Phase of the Migraine Attack; 2. Further Analysis of the Pain Mechanisms in Headache, Arch. Neurol. & Psychiat. **63**:42 (Jan.) 1950.

75. Huerkamp, B., and Rittinghaus, F. W.: Über die Blutversorgung der menschlichen Retina unter der Einwirkung veränderter Sauerstoffspannung, von Kohlensäure, Hyperventilation und Adrenalin, Arch. ges. Physiol. **252**:312, 1950.

76. Bietti, G. B., and de Gaspare, F.: Gli effetti dell 'inalazione di ossigeno su zone scotomatose del camp visivo, Boll. ocul. **29**:29, 1950.

mainly on the Bjerrum screen placed at a distance of 2 meters. Tests were also done on the perimeter and the angioscotometer. It was found that there was a reduction in the visual field defects caused by glaucoma, optic nerve atrophy, amblyopia and hemianopic lesions of central origin. These improvements were extremely transitory. No constant relationship was found between the enlargement of the visual field and the age of the ocular or nervous lesions. Inhalation of oxygen produced little or no effect on the visual field changes in peripapillary degeneration of myopia, retinal detachment, retinitis pigmentosa or thrombosis of the central retinal vein. Dubois-Poulsen, Leroy and Couzi [77] investigated the effect of intramuscular injections of acetylcholine on angioscotomas and retinal arterial pressure. They found that intramuscular injections of 2 mg. of acetylcholine produced only equivocable changes in the retinal vessels. Intravenous injections of sufficient amounts of acetylcholine to produce shock—up to ½ grain (0.032 Gm.)—caused a marked transitory reduction in the arterial pulse with a secondary rise. When the patient recovered from shock, his vessels returned to normal size.

Castagno [78] found that 2 per cent homatropine hydrobromide instilled into the conjunctival sac produced a measurable increase in the area of angioscotoma in 11 eyes of 10 subjects. This was not related to the dilatation of the pupils, the change in blood pressure or pulse rate or the pH of the solution used. Homatropine instilled into one eye did not affect the angioscotoma of the other eye.

Weigelin and Freusberg [79] discuss the origin of errors in comparing ophthalmodynamometric readings of the retinal vessels with the brachial arterial pressure. In their study attention is called to the fact that ophthalmodynamometric data, expressed in grams, cannot be compared directly with brachial arterial pressure, expressed in millimeters of mercury. They show that the various formulas which have been used to convert these findings vary greatly when readings are taken on hypertensive patients. They also point out that the relation of diastolic retinal arterial pressure to diastolic brachial arterial pressure is subject to wide physiological variations. Therefore, it is not permissible to draw any conclusion as to the condition of the general circulatory system from ophthalmodynamometric readings.

Weigelin and Niesel [80] investigated the influence of various body positions on the retinal arterial pressure by means of ophthalmodynamometry. An investigation of 250 normal healthy patients showed that any changes in body position might lead to a change in the blood pressure of the central retinal arteries. The greatest change, however, was found when the position was changed from vertical (sitting or standing) to horizontal (lying). The diastolic pressure was 7.5 mm. of mercury greater in the lying than in the standing or sitting position.

Hollenhorst and Wagener [81] review the literature on the loss of vision following distant hemorrhage and report five new cases in which this phenomenon had

77. Dubois-Poulsen, A.; Leroy, J., and Couzi, J.: Quelques données nouvelles sur l'action physiologique oculaire de l'acétylcholine, Ann. ocul. **183**:265, 1950.

78. Castagno, M. M.: The Effect of the Local Use of Homatropine Hydrobromide on the Normal Angioscotoma, Am. J. Ophth. **33**:367, 1950.

79. Weigelin, E., and Freusberg, O.: Über die Masseinheiten der Dynamometrie, Ophthalmologica **119**:292, 1950.

80. Weigelin, E., and Niesel, P.: Der Netzhautarteriendruck bei Änderung der Körperlage, von Graefes Arch. Ophth. **150**:374, 1950.

81. Hollenhorst, R. W., and Wagener, H. P.: Loss of Vision After Distant Hemorrhage, Am. J. M. Sc. **219**:209, 1950.

occurred. They discuss the mechanism of loss of vision and conclude that the essential factor was anoxia, which at times affected the retina, optic nerve or higher visual pathways. Loss of vision occurred more frequently after multiple small hemorrhages than it did after a single massive hemorrhage. There was frequently an interval of several days between the loss of blood and the loss of vision.

A sudden loss of vision occurred from bilateral retinal arterial spasm in a 23 year old man 24 hours after a severe hemorrhage following subtotal thyroidectomy (Grossmann and Holm [82]). An immediate transfusion, 100 mg. of nicotinic acid four times a day and 0.5 grain (0.032 Gm.) of erythrityl ("erythrol") tetranitrate four times a day produced no improvement in his vision. Nine days after the onset of his lesion a bilateral stellate ganglion block with procaine produced improvement in the vision in one eye within two minutes.

Jaensch [83] discusses the use of benzazoline (priscol®) in disease of the retina and optic nerve. He believes that daily intramuscular injections of this substance for a month during the early stages of amblyopia and retrobulbar neuritis due to methyl alcohol poisoning relieved retinal vascular spasm and resulted in improvement of visual acuity. Good results were also obtained with this drug in relaxing spasm of the central retinal artery in young adults. Lesions which had existed for a long time were not improved by this method of treatment.

Fuchs [84] describes the case of a man aged 48 with endangiitis obliterans. The patient, first seen in February 1949, gave a history of pronounced failure of vision in his right eye since June 1948 and complete loss of vision in this eye in December 1948. Three weeks before observation there had been diminution of vision in the left eye. On examination, the right fundus could not be seen because of a cataract. Vision was limited to faulty light projection. Ophthalmoscopic examination of the left eye revealed greatly attenuated arteries with sausage-shaped, saccular dilatations. In places the blood in the veins presented a boxcar appearance. Glyceryl trinitrate was given, and acetylcholine and neostigmine methylsulfate were injected. The patient's vision improved from 5/36 to 5/12, and the vessels assumed a more normal appearance. After two weeks the injections had no further effect. Block of the stellate ganglion was effected by 10 cc. of 2 per cent procaine hydrochloride, and the patient's vision again improved from 5/36 to 5/12, with accompanying dilatation of the retinal arteries. A cataract developed in the left eye two months after the patient was discharged from the hospital.

Müller [85] reports the case of a man aged 28, who died 18 hours after the injection of methyl alcohol. Histological examination revealed numerous cystic spaces in the inner and outer plexiform layers in the posterior portion of the retina, acute toxic hydrops of the inner nuclear layer and a large transudation from the choriocapillaris and retinal capillaries. In places the pigment epithelium was detached and thrown into folds. The ganglion cells appeared normal.

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82. Grossmann, E. E., and Holm, A. G.: Amblyopia After Thyroidectomy, Am. J. Ophth. **33**:1099, 1950.

83. Jaensch, P. A., and Budde, H.: Priscol bei Erkrankungen der Netzhaut und des Sehnerven, Klin. Monatsbl. Augenh. **116**:267, 1950.

84. Fuchs, J.: Über sichtbare Blutströmung in den Netzhautvenen bei Endangitis obliterans, Klin. Monatsbl. Augenh. **117**:253, 1950.

85. Müller, H.: Histologische Untersuchung eines Auges bei akuter tödlicher Methylalkoholvergiftung, Klin. Monatsbl. Augenh. **116**:135, 1950.

Nagy [86] observed two patients with polycythemia vera—a man aged 24 and a woman aged 40, who had blood pressures of 150 and 170 mm., respectively. In both patients he observed transitory attacks of spasm of the central retinal artery, which resulted in marked reduction in visual acuity. On two occasions these spasms were photographed. On one examination, all the arteries in the fundus became white, threadlike structures, and the smaller arteries disappeared. After 10 to 15 minutes the vessels regained their patency. Visual acuity during the spasm was reduced to perception of hand motions. Two weeks later the visual acuity was 5/20. This is an interesting observation, for ordinarily a patient would not be expected to regain vision after total occlusion of the central retinal artery for 10 to 15 minutes.

Donahue [87] presents an excellent review of the history, incidence, etiology, clinical types, ocular complications and pathogenesis of ocular symptoms arising from migraine. Visual disorders in the form of scintillating scotomas and fortification spectrums occurred in 54 per cent of the cases reported. Hemianopsia, both transverse and vertical, occurred in 4 per cent. Central scotomas were rare. These lesions were thought to be due to cerebral angiospasm. Edema of the retina and retinal hemorrhages were recorded in a number of cases. Thrombosis of the retinal vessels was rarely recorded.

Four cases of retinal arterial occlusion occurring in patients with migraine are reported by Graveson.[88] In one patient the central artery of the retina was affected, and in three the occlusion occurred in a single peripheral branch. The author believes that such cases provide evidence for the theory that the preheadache phenomena of migraine are due to vasospasm.

Turnbull [89] produced retinal anoxia in rats by several ingenious methods. He sectioned the central retinal artery, centrifuged the animals for three minutes at 10 G with their heads facing inward and asphyxiated them with nitrogen gas for three minutes. The retinas were found to be edematous almost immediately after these procedures. Irreversible changes occurred in the ganglion cells within four to five hours, and complete loss of the nerve fiber and ganglion cell layers occurred on the seventh postoperative day.

CENTRAL VEIN THROMBOSIS

During the past few years there has been considerable discussion as to the value of anticoagulants in treatment of thrombosis of the central vein. The most obvious defect in evaluation of the efficiency of these drugs has been the lack of an adequately studied large series of patients who have not received anticoagulants. In the past year two reports have appeared which are of value in the attempt to settle this controversy.

In an extensive monograph, Braendstrup [90] discusses the nature of the disease and reviews the histories of 131 patients with thrombosis of the central vein who

86. Nagy, F.: Changes in the Fundus Caused by Polycythemia, Brit. J. Ophth. **34**:380, 1950.

87. Donahue, H. C.: Migraine and Its Ocular Manifestations, Arch. Ophth. **43**:96 (Jan.) 1950.

88. Graveson, G. S.: Retinal Arterial Occlusion in Migraine, Brit. M. J. **2**:838, 1949.

89. Turnbull, W.: Effects of Experimental Retinal Anemia in Rats, Arch. Ophth. **43**:9 (Jan.) 1950.

90. Braendstrup, P.: Central Retinal Vein Thrombosis and Hemorrhagic Glaucoma, Acta ophth., supp. 35, 1950.

had been seen or hospitalized in one of two large Danish eye clinics. None of these patients were treated with anticoagulants. Eighty of the 131 patients were men, and 51 were women. The left eye was affected in 74 patients and the right eye in 48. In 8 patients the lesion was bilateral. Their ages ranged from 20 to 89 years, the highest incidence occurring between the ages of 65 and 75. The prodromal symptoms were indefinite and did not differ from those that occur in a great number of persons who have the same degree of vascular sclerosis and in whom thrombosis of the central vein does not develop. Information from the patients' histories indicated that the onset of the disease was sudden. Sixty-five patients reported to the eye clinics after the onset of their symptoms without having had previous ocular complications. Twenty of these patients were examined within two weeks after the onset of symptoms, and 36, within a month. The visual acuity was recorded for 58 of the 65 patients. In 15 it was found to be better than 20/60; in one-half, better than 20/200. The primary cause of the disease was thought to be arteriosclerosis, which produced either a true thrombus or endothelial proliferation in the vein. In 82 of the 131 patients there were symptoms of cardiovascular disease, as judged by the condition of the retinal vessels in the unaffected eye or by myocardial or renal lesions. Eight of the patients were normal except for a systolic blood pressure of 150 to 175 mm. Eighteen of the patients showed no physical abnormality other than their central vein thrombosis. Information on 23 of the patients was not sufficient to permit a conclusion as to the state of their cardiovascular condition.

In the overwhelming majority of cases, restoration of blood circulation took place either through visible anastomoses on the papillae or through recanalization of the central retinal vein. The average time for reabsorption of the hemorrhage was approximately one to two years. Reactivation of the hemorrhage after the first extravasation was rare. Evidence of previous venous occlusion was present in all fundi that healed. In practically all the patients there was evidence of sclerosis of both the artery and the vein; sheathing of the vein was noted in 14 cases, and new-formed vessels were seen on the optic disk in 75 per cent of the eyes. Loss of vision was due primarily to macular degeneration.

That the primary ocular tension was frequently lower than normal offered little indication as to whether hemorrhagic glaucoma would develop. Hemorrhagic glaucoma occurred in 62 of the 131 patients, but the author notes the probability that this incidence is higher than in general practice because more of the patients with complications were referred to the hospital for care. The onset of the glaucoma occurred within six months after the thrombosis of the central vein in 66 per cent of the patients, and in the majority of these it occurred within three months.

The final visual result was recorded for 50 of the 69 patients in whom hemorrhagic glaucoma did not develop (table 1). All but 9 of the patients were followed until the hemorrhages had absorbed, and 7 of these 9 patients were in the group that obtained less than 20/400 vision.

One could not always prognosticate the final visual acuity from the extent of the hemorrhage when the patient was first seen. There was a correlation, however, between good visual acuity at the onset of the disease and good final visual acuity, although some of the patients with primary good function obtained only moderate results. With one exception, all the patients who obtained better than 20/60 vision were between the ages of 25 and 54.

In a second series, from the Eye clinic of Lund, Sweden, all the patients with thrombosis of the retinal vein were treated with anticoagulants. The dose of heparin used was 25 mg. twice daily for 10 to 21 days. When bishydroxycoumarin U.S.P. (dicumarol®) was administered, the prothrombin index was tested daily and was not allowed to pass 40 to 50. One hundred patients were treated in this manner, 59 of whom had thrombosis of the central vein and 41 thrombosis of tributary veins. Larsson and Nord [91] report the results of these cases. The final visual acuity is charted in table 1.

An exact comparison of the untreated series of Braendstrup and the treated series of Larsson and Nord is not possible when expressed in Snellen's figures, for the metric system was used to record the visual acuity in the untreated series and the International System in the treated series. However, an approximate comparison reveals that 16, or 32 per cent, of the untreated patients and 27, or 46 per cent, of the treated patients obtained 20/90 vision or better. Ten, or 20 per cent, of the untreated patients obtained 10/200 vision or better, and 10, or 17 per cent, of the treated patients obtained this vision. Twenty-four, or 48 per cent, of the untreated and 22, or 37 per cent, of the treated patients acquired less than 20/200 vision. These workers concluded that while heparin and dicumarol® therapy offered tempting possibilities from a theoretical point of view, this form of treatment had far from revolutionized the management of patients with thrombosis of the central vein.

TABLE 1.—*Visual Results Following Thrombosis of the Central Vein*

50 Cases (Braendstrup [90]) No Anticoagulant Therapy		59 Cases (Larsson and Nord [91]) Anticoagulant Therapy	
No. of Patients	Final Vision*	No. of Patients	Final Vision†
11	20/30 or better	11	20/25 or better
3	20/80 or better	10	20/50 or better
8	20/200 or better	12	20/200 or better
4	10/200-20/200	4	10/200-20/200
24	Less than 10/200	22	Less than 10/200

* Converted from metric system.
† Converted from international system.

Klien [92] reports the use of heparin and dicumarol® therapy in four patients with thrombosis of the central vein. Three of these patients obtained 20/20 vision or better. Two of the patients suffered renal hemorrhage during therapy, and in one of these the erythrocyte count fell to 1,600,000. Klien reduced the prothrombin level lower and continued the treatment longer than did Larsson and Nord. She also points out the necessity for close observation of the prothrombin level and recommends hospitalization during the initial stages of therapy.

Damel and Brodsky [93] report observations on 39 patients with thrombosis of the central vein. They describe the appearance of the fundus in various stages of this disease. Baurmann [94] studied the retinal venous pulsation by ophthalmodynamometry in patients with occlusion of the central retinal vein and concluded that when

91. Larsson, S., and Nord, B.: Some Remarks on Retinal Vein Thrombosis and Its Treatment with Anticoagulants, Acta ophth. **28**:187, 1950.

92. Klien, B. A.: Prevention of Retinal Venous Occlusion, Am. J. Ophth. **33**:175, 1950.

93. Damel, C. S., and Brodsky, M.: Oclusión de la vena central de la retina (evolución oftalmoscópica), Arch. Soc. oftal. hispano-am. **10**:21, 1950.

94. Baurmann, M.: Venenpulsbeobachtungen bei Entstehung und Heilung von Zentralvenenverschluss, Klin. Monatsbl. Augenh. **116**:461, 1950.

high pressure was needed to produce venous thrombosis the prognosis was poor. Braendstrup [90] considers this test of little value in prognosticating the final outcome of this type of lesion. Benedict [95] correlated the age, incidence and other vascular complications with closure of the central retinal vessels in 500 cases. In 132 of these cases there was closure of the central retinal artery, and in 367 cases, closure of the central vein or its tributaries. In five cases the venous thrombosis was bilateral, and in seven cases there was occlusion of both the vein and the artery. Secondary glaucoma occurred in 41, or 11.4 per cent, of the cases of venous thrombosis and in one of the cases of occlusion of the central vein. The age, incidence of occlusion of the central artery and incidence of occlusion of the central vein or a tributary branch are given in table 2.

The incidence of cardiovascular disease was surprisingly low in this series. In 39.4 per cent of the patients with closure of the retinal artery there was arteriosclerosis, hypertension, coronary disease or a cerebral accident. Only 25.5 per cent of the patients with closure of the retinal vein had these complications.

DeVoe [96] describes the case of a man aged 25 with fat emboli of the retinal vessels, who was struck by an automobile and suffered multiple compound com-

TABLE 2.—*Age of Patients with Occlusion of Central Artery and Occlusion of Central Vein or of a Tributary Branch*

Arterial Occlusion		Venous Occlusion	
No. of Patients (132)	Age, Yr.	No. of Patients (361)	Age, Yr.
10, or 7.6%	Below 29	13, or 3.6%	Below 29
12, or 9.1%	30-39	15, or 4.2%	30-39
19, or 14.4%	40-49	57, or 15.8%	40-49
39, or 29.9%	50-59	102, or 28.3%	50-59
52, or 39.3%	Above 60	174, or 48.2%	Above 60

minuted and simple fractures of both tibias and fibulas, fractures of the eleventh rib on the right side and fractures of the transverse processes of the first to the fourth lumbar vertebrae. There was no head injury. The patient died 2½ days after injury. Examination of his eyes 18 hours before death showed multiple petechial hemorrhages in the conjunctiva of both eyes. The disk of the right eye was normal, and no gross abnormalities could be detected in the retinal vasculature. There was a cherry-red spot in the fovea, surrounded by an area of edema. Adjacent to this were six discrete, fluffy exudates of fresh cotton-wool type. No hemorrhages were present. The left eye presented a similar picture. Autopsy revealed massive fat emboli of the capillaries and venules in all organs, as well as fat globules within the alveoli of the lungs and lumens of the renal tubules. Histological examination of the eyes showed globules of fat at irregular intervals in the choroidal vessels. Many superficially situated vessels in the retina were also occluded by fat. In the macular area several occluded vessels were surrounded by edematous, disorganized retinal tissue. The abnormal retinal tissue was thought to correspond to the cotton-wool patches seen ophthalmoscopically.

95. Benedict, W. L.: The Clinical Significance of Closure of the Retinal Vessels, J. M. A. Georgia **38**:423, 1949.

96. DeVoe, A. G.: Ocular Fat Embolism: A Clinical and Pathologic Report, Arch. Ophth. **43**:857 (May) 1950.

DIABETIC RETINOPATHY

Joslin and Wilson [97] found that the average life span of 135 diabetic children who died in the period from 1944 to 1949 exceeded by approximately eight years the average life span of those who died in the six previous years, 1937 to 1943. Comparison of the causes of death in 157 children who died between 1908 and 1922 with the causes in 135 children who died between 1944 and 1949 show striking differences. In the preinsulin era, 86 per cent died of diabetic coma, and 6.4 per cent died of infections. Of the more recent group, 9.6 per cent died of diabetic coma, 59. 3 per cent of cardiorenal vascular disease, 7.4 per cent of infections and 11.9 per cent of tuberculosis. Sixty per cent of these children had retinopathy, and five (4 per cent), retinitis proliferans.

During the past few years the nature of the retinal vascular lesion has been considerably clarified by the work of Ballantyne and Loewenstein [98] and Friedenwald.[99] It is now well established that the persistent round, punctate lesions seen in diabetic retinopathy are either microaneurysms or small hemorrhages surrounding aneurysms in the inner nuclear layer of the retina. Friedenwald stained flat preparations of the retinas in 67 cases of diabetes with the Hotchkiss-McManus (periodic acid-Schiff reagent) technic and found that 43 of them showed capillary aneurysms, mainly in the region of the disk and macula. The average duration of diabetes in these cases was 13 years. The majority of the lesions were 20 to 30 microns in diameter and were located at bifurcations or sharp bends on the venous side of the capillaries.

The frequency with which capillary aneurysms are found in the retinas of patients with long-standing diabetes suggests that these lesions may be fundamentally related to the systemic vascular degeneration which occurs in diabetics. Ashton [100] examined the choroid, ciliary body, iris, conjunctiva, brain, meninges, pleura, pericardium, omentum, peritoneum, bladder mucosa and capsules of the kidney and liver and failed to find any similar lesions. Friedenwald,[99b] with Day, examined the conjunctiva of 60 diabetics and the nail beds of 40 diabetics with the corneal microscope but were not able to find lesions which were unquestionably comparable to those seen in the fundus. There does seem to be a relationship, however, between "intercapillary glomerular sclerosis" and the retinal lesions in patients with long-standing diabetes. Thus, Friedenwald and Day [99b] found that of 43 diabetic patients with retinal capillary aneurysms, 25 showed typical nodular hyaline deposits in their renal glomeruli, while 33 diabetic patients with no retinal capillary aneurysms showed no characteristic renal lesions. Ashton [100] reports a similar incidence in a smaller series. Of 21 diabetics studied, 12 showed capillary aneurysms in the retina, and of these 12, seven were found to have the characteristic renal lesions. None of the nine without retinopathy showed the characteristic nephropathy. There was, however, no exact correlation between the severity of the retinal and that of the renal lesions.

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97. Joslin, E. P., and Wilson, J. L.: Lessons for Future Treatment from 472 Fatalities in Diabetic Children, Brit. M. J. **2**:1293, 1950.

98. Ballantyne, A. J., and Loewenstein, A.: Diseases of the Retina: I. The Pathology of Diabetic Retinopathy, Tr. Ophth. Soc. U. Kingdom (1943) **63**:95, 1944; Micro-Aneurysms and Punctate Hemorrhages, Brit. J. Ophth. **28**:593, 1944.

99. (*a*) Friedenwald, J. S.: A New Approach to Some Problems of Retinal Vascular Disease, Am. J. Ophth. **32**:487, 1949; (*b*) Diabetic Retinopathy, ibid. **33**:1187, 1950.

100. Ashton, N.: Vascular Changes in Diabetes with Particular Reference to the Retinal Vessels: Preliminary Report, Brit. J. Ophth. **33**:407, 1949.

Alwall, Ekelund and Oras [101] state that retinopathy was noted in 93 per cent of the 89 cases of the Kimmelstiel-Wilson syndrome (intercapillary glomerulosclerosis) reported in the literature. They present their autopsy findings in five cases of this syndrome.

Ashton [100] made extensive comparisons of the staining characteristics of the retinal and the glomerular hyalin and concluded that the two materials are strikingly similar. He also added a refinement to Friedenwald's use of the Hotchkiss-McManus stain on the retinal blood vessels by counterstaining with benzidine, which colors blue the red blood cells inside the capillary aneurysms.

Friedenwald points out that, while the capillary aneurysms in diabetic retinopathy are extremely persistent, there are exacerbations and remissions of the fundus lesions. This characteristic should be remembered in attempting to evaluate therapy, for such improvement may give rise to false hopes. Ascorbic acid, rutin and moccasin venom appear to have little effect on the progress of diabetic retinopathy.

Capillary aneurysms are occasionally found in the retina in cases of hypertension and thrombosis of the central retinal vein. However, in these conditions the lesions tend to be located in the periphery rather than in the macular area of the retina. In hypertensive retinopathy the aneurysms are on the arterial, rather than the venous, side of the capillaries. Wexler and Branower [102] stained flat preparations of the retina from 53 eyes with the periodic acid-Schiff reagent technique (Hotchkiss-McManus stain). Thirteen of the patients were diabetic. Eleven had malignant hypertension and malignant nephrosclerosis, and 29 had nonmalignant hypertension. The findings in the diabetic patients were essentially those that have been described by Ballantyne, Friedenwald and Ashton. The retinas of all eyes from patients with hypertensive disease in the malignant phase showed dilated and saccular arterial capillaries, similar to those seen on the venous side of the capillaries in diabetes. There was also a focal duplication of the basement membrane at the point of sacculation. In only 1 of the 29 cases of nonmalignant hypertensive disease were significant capillary lesions seen.

LIPEMIA RETINALIS

Lipemia retinalis is a not infrequent occurrence in poorly controlled diabetes, but nondiabetic lipemia of the retina is thought to be rare. Only eight cases had been cited in the literature prior to 1950. During this year six additional cases have been reported. Dunphy [103] discusses hyperlipemia and points out that Niemann-Pick disease, Tay-Sachs disease, Goucher's disease and the Schüller-Christian syndrome represent systemic disturbances of the intracellular fat metabolism. Thannhauser [104] classifies hyperlipemia, other than the physiological form which occurs after eating a fatty meal, into two types: (1) transportation hyperlipemia, which occurs in diabetes, chronic alcoholism, acute starvation, severe anemias, leukemias, lipid nephrosis and poisoning with agents, such as phosphorus, chloroform and carbon tetrachloride, which damage the liver; (2) retention lipemia, which is thought to be due to an accumulation of fat in the pancreas, interfering with its

101. Alwall, N.; Ekelund, C., and Oras, L.: Intercapillary Glomerulosclerosis (Kimmelstiel-Wilson's Disease), Acta med. scandinav. **136**:359, 1950.

102. Wexler, D., and Branower, G.: Retinal Capillary Lesions in Malignant Hypertension, Arch. Ophth. **44**:539 (Oct.) 1950.

103. Dunphy, E. B.: Idiopathic Hyperlipemia, Am. J. Ophth. **33**:1579, 1950.

104. Thannhauser, S. J.: Medical Progress: Serum Lipids and Their Value in Diagnosis, New England J. Med. **237**:515, 1947.

function. Insulin has no effect on the level of the neutral fat in this condition, as it does in diabetes. The latter condition is spoken of as idiopathic hyperlipemia.

The total fatty acid content of the serum is made up of three compounds: the fatty acids of the phospholipids, the cholesterol esters and the neutral fats. An increase in the total fatty acids may be due to a rise in any or all of these fractions. Dunphy points out that the neutral fats must be increased before fat can be seen in the retinal vessels. Thus, the total cholesterols may be high, but unless the neutral fat is also high there will be no lipemia retinalis. He reports the case of a man aged 47 who had idiopathic hyperlipemia. On three occasions when the patient's fasting neutral fat blood level became elevated above 2,500 mg. per 100 cc. lipemia retinalis developed. When he was placed on a low fat diet, his blood lipid level was reduced, and fat could no longer be seen in the retinal blood vessels. A second patient, who had idiopathic hyperlipemia and lipid interstitial keratitis, was also studied. This patient's neutral fat serum level was elevated to 1,832 mg. per 100 cc., and lipemia retinalis did not develop.

Three other cases of nondiabetic hyperlipemia are reported by Groom and Rucker.[105] One patient, a white man aged 59, had idiopathic hyperlipemia with a fasting total plasma lipid level of 3,584 mg. per 100 cc. When he was placed on a low fat diet, the retinal vessels assumed their normal appearance, and the total plasma lipid content fell to 1,872 mg. per 100 cc. (normal, 400 to 650 mg. per 100 cc.). Their second patient was a white man aged 32 with chronic alcoholism who had a total lipid content of 4,740 mg. per 100 cc. After four days' hospitalization and a high carbohydrate, high vitamin diet, the condition of the fundi returned to normal. Their third patient was a white male infant aged 7 months who had a total lipid content of 5,242 mg. per 100 cc. The diagnosis in this case was Niemann-Pick disease.

The sixth case of nondiabetic lipemia retinalis is reported by Lewis.[106] A woman aged 47 had obvious liver damage. Her left fundus was normal. In her right eye there were widely scattered yellowish patches. These were found in the deeper layers of the retina. The lesions varied in size from 5 D. to large, confluent masses. The largest mass formed an extensive tumor involving the lower one sixth of the fundus, producing a detachment of the retina over it.

PROLIFERATIVE VASCULAR CHANGES

Intramural vessels are found in the ascending aorta and in sclerosed coronary arteries. These vessels have not previously been described in the retina. Loewenstein[107] demonstrated intramural vessels in the arteries and veins of the retina in cases of arteriosclerosis with hypertension, diabetic retinopathy and thrombosis of the central retinal vein. He also found them in three cases of periarteritis nodosa and in two cases of vasculitis in young adults with hemorrhage in the retina and vitreous.

105. Groom, J. J., and Rucker, C. W.: Nondiabetic Lipemia Retinalis, Am. J. Ophth. **33**: 1238, 1950.

106. Lewis, N.: Intraocular Involvement in a Case of Xanthomatous Biliary Cirrhosis, Brit. J. Ophth. **34**:506, 1950.

107. Loewenstein, A.: Intramural Vessels and Endothelial Cells in the Walls of Sclerosed Retinal Arteries, Brit. J. Ophth. **34**:594, 1950.

Ballantyne [108] describes new-formed vessels in the fundus. Clinically, they are of four types: (1) new-formed vessels in the retina (intraretinal, periretinal or in the vitreous chamber); (2) new-formed vessels in the optic disk; (3) chorioretinal anastomoses, and (4) new-formed subretinal vessels. Some of these new-formed channels, especially those in the intraretinal situation, may arise by the pathological expansion of preexisting capillaries, but in the majority of cases new-formed vessels arise by budding of the retinal and choroidal system. The great majority of new-formed vessels have their origin from the venous side of the capillaries and are associated with thrombosis or some other type of venous obstruction. In some instances, however, they arise from the arteries, and in others they occur as a result of arteriovenous anastomosis. The new-formed capillaries arise in venous obstruction to produce collateral channels of circulation. In other instances their appearance seems to result from an attempt to improve the nutrition in a pathological area or to aid in the removal of irritating substances, such as hemorrhages and exudates. Anastomosis of the chorioretinal vessels usually occurs in old scars where there has been destruction of the choroid and retina from inflammatory processes.

TREATMENT OF RETINAL VASCULAR LESIONS

Woods [28] reports that a disciform degeneration of the macula with hemorrhages and exudates improved when the patient was given ACTH. Steffensen and his co-workers [109] report similar improvement in the case of a man aged 48 with central serous retinopathy. Woods [110] reports two cases of retinal periphlebitis with retinal and vitreous hemorrhages which improved on streptomycin and thiazolsulfone (promizole®) therapy. Bietti [111] reported a similar response of retinal periphlebitis to streptomycin and paraaminosalicylic acid treatment.

TRAUMA

A symposium on ocular injuries was presented before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association in 1949, at the request of the Surgeon General. Stone [112] stated that the eye was involved in approximately 2 per cent of the combatant and noncombatant injuries in World War II. These injuries resulted in at least 14,900 cases of decidely impaired vision or blindness in one or both eyes. Five thousand and fourteen of these eyes had been enucleated by the end of 1945 as a result of these lesions. The percentage of retinal lesions in these cases was not mentioned. Payne,[113] Marshall [114] and

108. Ballantyne, A. J.: New-Formed Vessels in the Fundus Oculi, Ophthalmologica **118**: 611, 1949.

109. Steffensen, E. H.; Olson, J. A.; Margulis, R. R.; Smith, R. W., and Whitney, E. L.: Experimental Use of Cortisone in Inflammatory Eye Disease, Am. J. Ophth. **33**:1033, 1950.

110. Woods, A. C.: Therapeutic Action of Streptomycin and Promizole® in Clinical Ocular Tuberculosis: A Preliminary Report, Arch. Ophth. **42**:521 (Nov.) 1949.

111. Bietti, G. B.: Use of Paraaminosalicylic Acid Alone or in Association with Streptomycin in Ocular Tuberculosis: Experimental and Clinical Investigations, Arch. Ophth. **43**:431 (March) 1950.

112. Stone, W.: Ocular Injuries in the Armed Forces, J. A. M. A. **142**:151 (Jan. 21) 1950.

113. Payne, B. F.: Ocular Contusions in National Emergencies, J. A. M. A. **142**:243 (Jan. 28) 1950.

114. Marshall, D.: Lacerations and Perforations of the Lids and Globe, J. A. M. A. **142**: 246 (Jan. 28) 1950.

Callahan [115] note that vitreous and retinal hemorrhages, retinitis proliferans, edema of the retina, macular holes and detachment of the retina occurred as a result of contusions, lacerations of the globe and intraocular foreign bodies. Lesions of the eye from radiant energy are discussed by Cogan.[116] He mentions that local application of diathermy waves may produce a thermal coagulation of the retina. The long infrared rays probably cause no damage to the retina because they are absorbed in the anterior portion of the eye. The short infrared rays and the visible rays can cause thermal burns of the retina because they not only reach the retina but are refracted by the ocular media. The ultraviolet wave band has not been shown to produce any organic lesion in the retina. The neural elements of the retina are relatively resistant to roentgen and gamma rays. However, a sufficient dose of these rays may cause chromatolysis of the ganglion cells and sclerosis of the retinal vessels.

The effect of microwave diathermy (wavelength about 12 cm.) on the eye was studied by Daily and associates.[117] Exposure of rabbit eyes to microwaves which produced an average rise in temperature of 1.9 degree (C.) in the orbit, 3.2 degree (C.) in the vitreous and 2.8 degrees (C.) in the aqueous resulted in no lesions that could be seen on clinical or pathological examination. When the dose of radiation was increased slightly, however, typical thermal burns were produced in the cornea, lens and retina.

Twenty-four male and 32 female mice of strain A were given a single dose of 400 r (x-rays) to the whole body at birth.[118] The experiment was terminated 12 months later. Seventeen males and 22 females survived. All animals showed lesions in one or both eyes. Histologically, the most consistent and severest damage was seen in the retina. Almost no nuclei were present in the outer nuclear layer. The layer of rods (no cones are found in the eye of the mouse) was absent. The inner nuclear layer was reduced in thickness, and there was relatively little injury to the ganglion cell layer. The notable changes in the retina were thought to be due to the fact that this layer of the newborn mouse is not fully developed and contains an outer, undifferentiated layer. In addition to the retinal changes, opacities appeared in the lens, and partial opacification and vascularization of the cornea occurred.

Chance, Merritt and Bellows [119] studied the fundi of 839 infants with dilated pupils within a few days after birth. They found retinal hemorrhages in only 22, or 2.6 per cent, of their cases. The incidence of retinal hemorrhage in the first three days after birth was somewhat higher (4.5 per cent) than in the infants who were examined later (1.4 per cent).

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115. Callahan, A.: Foreign Bodies of the Eye, J. A. M. A. **142**:249 (Jan. 28) 1950.

116. Cogan, D. G.: Lesions of the Eye from Radiant Energy, J. A. M. A. **142**:145 (Jan. 21) 1950.

117. Daily, L. Jr.; Wakim, K. G.; Herrick, J. F.; Parkhill, E. M., and Benedict, W. L.: Effects of Microwave Diathermy on the Eye, Am. J. Ophth. **33**:1241, 1950.

118. Lorenz, E., and Dunn, T. B.: Ocular Lesions Induced by Acute Exposure of the Whole Body of Newborn Mice to Roentgen Radiation, Arch. Ophth. **43**:742 (April) 1950.

119. Chace, R. R.; Merritt, K. K., and Bellows, M.: Ocular Findings in the Newborn Infant: A Preliminary Report, Arch. Ophth. **44**:236 (Aug.) 1950.

RETINAL DETACHMENT

One of the most important steps in successful surgical measures for retinal reattachment is a careful examination of the detached retina. Numerous workers have shown that the percentage of good results is in direct proportion to the discovery and localization of retinal tears and holes. Since many of these lesions are located in the far periphery of the fundus, it is of value to use the method of ophthalmoscopy which gives the clearest view of the periphery of the retina. Schepens and Bahn [120] discuss the examination of the ora serrata with direct and indirect ophthalmoscopy. They found and used as landmarks pathological lesions in the anterior retina in seven eyes. The extent of clear visibility was 1 to 3 disk diameters greater with indirect than with direct ophthalmoscopy. This difference was thought to be due to the fact that the apex of the light cone in direct ophthalmoscopy is located at some distance from the pupil, whereas the apex of the cone of illumination may be placed in the pupillary space when indirect ophthalmoscopy with a + 20.00 D. lens is used. This variation becomes of great importance in examining the extreme periphery of the fundus, because the pupil when viewed obliquely is reduced to a slit. The authors suggest that there is a close relationship between the amount of distortion and the magnification of the retinal image. Magnification with the direct ophthalmoscope in an emmetropic fundus is approximately 15 times, but with a + 20.00 D. condensing lens and a + 3.00 D. lens in front of the observer's eye the magnification is only about 2.2 times. The appearance of retinal dialyses near the ora serrata as viewed with indirect ophthalmoscopy is described in two aphakic eyes and two phakic eyes.

Arruga [121] examined 200 eyes with retinal detachments with both indirect and direct ophthalmoscopy. He was able to find tears with either method in 154 cases, with indirect but not with direct ophthalmoscopy in 25 cases, and with direct but not with indirect ophthalmoscopy in 3 cases. Lesions near the ora serrata could be seen only with indirect ophthalmoscopy, whereas slitlike tears in folds of detached retina could be visualized only with direct ophthalmoscopy.

A number of workers have discussed the methods of treatment and the factors which influence the final results in patients with retinal detachments.[122] The percentage of cures varies from 25 to 93, depending on the type of operation used and the selection of cases for operation.

Shapland [123] reports that of 221 eyes treated by the Gonin cautery puncture there was a cure in 30 per cent. The Guist-Linder multiple trephine operation and chemical cauterization resulted in successes in 28 per cent of 78 cases. Superficial and multiple puncture diathermy resulted in reattachments in 61 per cent of 155 eyes. The factors which influenced the final results of reattachment surgery were the

120. Schepens, C. L., and Bahn, G. C.: Examination of the Ora Serrata: Its Importance in Retinal Detachment, Arch. Ophth. **44**:677 (Nov.) 1950.

121. Arruga, H.: The Relative Importance of Direct and Indirect Ophthalmoscopic Examination in the Treatment of Retinal Detachment, Brit. J. Ophth. **33**:651, 1949.

122. Shipman, J. S.: Some Practical Facts Regarding Retinal Detachment Surgery, Am. J. Ophth. **33**:847, 1950. Cosmettatos, D. F.: Quelques considérations sur le décollement de la rétine, Ophthalmologica **118**:651, 1949. Arruga, H.: Quelques déductions à propos de deux mille cas de décollement de rétine opérés, ibid. **118**:655, 1949. Fink, A. I.: Detachment of the Retina in Young Adults, Am. J. Ophth. **33**:424, 1950. Koenig, I. J.: Failures in Retinal Detachment Surgery, New York J. Med. **49**:2405, 1949. Savin, L. H.: Detachment of the Retina, M. Press **224**:44, 1950.

123. Shapland, C. D.: Detachment of the Retina, M. Press **222**:605, 1949.

discovery of retinal tears, the size and location of the tears, the presence of active or inactive uveitis and the history of perforating injuries of the globe, traction bands in the vitreous, duration of the detachment, drainage of the subretinal fluid at the end of operation, position of the retina at the end of operation, age of the patient, refractive error and whether or not the eye was aphakic.

Leffertstra [124] examined 200 patients with disinsertions of the retina at the ora serrata and found that 88 per cent of the lesions were located in the outer temporal quadrant. Cysts were found in the retina in 23 per cent of the eyes, and the lesion was bilateral in 14 patients. Diathermy operations were performed on 213 eyes, with successful results in 199, or 93 per cent. Duke-Elder [125] reports a case of a man aged 44 in whom a congenital cyst of the retina in the outer temporal quadrant ruptured and produced a disinsertion of the retina with a retinal detachment. He reports this case because he had been unable to find definite proof that a dialysis may develop from the bursting of a cyst of the retina.

Borley [126] reviews the literature on scleral resections from 1903 to 1949. He describes an operative technique in detail and discusses the operative and postoperative complications. Twenty-eight operations resulted in 9 cures, 8 improvements and 11 failures. The result was classified as a cure when the retina was reattached either immediately or within several months after operation, regardless of the status of visual acuity. Indications for the operation were (1) a disproportion between the size of the retina and scleral envelope, (2) detachments which had not been cured by one or more diathermy operations, (3) detachments in aphakic eyes with vitreous strands or retinitis proliferans, (4) detachments resulting from trauma in which there were large disinsertions and (5) in certain cases, high myopia associated with progressive loss of vision and visual field in the absence of retinal detachment.

Lindner [127] describes five cases of retinal detachment in which cure had not been produced by previous diathermy or in which strands were present in the vitreous. In all five cases cure was by scleral resection. He also mentions that from 1944 to 1945 the shortening operation had been performed on 36 eyes in his clinic. At the time of the patient's discharge, the detachment was cured in 6 eyes, improved in 10, unchanged in 9 and worse in 11. He considers the following conditions indications for scleral resection: (1) aphakic eyes without detectible holes in the retina, (2) aphakic eyes in which previous diathermy had been without success, (3) detachments of the retina fixed by vitreous strands which would prevent reattachment and (4) detachments which had been operated on unsuccessfully several times by other methods. He offers helpful suggestions on the way a scleral resection should be done and points out that he had operated on the entire circumference of one eye in one session without complications. Weve [128] describes a suture for shortening the sclera without removing tissue.

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124. Leffertstra, L. J.: Disinsertions at the Ora Serrata, Ophthalmologica **119**:1, 1950.

125. Duke-Elder, S.: The Relation Between Peripheral Retinal Cysts and Dialyses, Brit. J. Ophth. **33**:388, 1949.

126. Borley, W. E.: The Scleral Resection (Eyeball-Shortening) Operation, Tr. Am. Ophth. Soc. **47**:462, 1949.

127. Lindner, K.: Shortening of the Eyeball for Detached Retina, Arch. Ophth. **42**:634 (Nov.) 1949.

128. Weve, H.: Bulbusverkürzung durch Reffung der Sclera, Ophthalmologica **118**:660, 1949.

The hyaluronic acid and hyaluronidase content of the subretinal fluid were estimated with a viscosimeter in 17 eyes with retinal detachment by Godtfredsen.[129] Hyaluronic acid was found in the subretinal fluid in all eyes with retinal tears but was not found in two eyes with retinal detachments secondary to melanoma. Hyaluronidase was not demonstrated in the subretinal fluid of any of the eyes. These results were thought to be further evidence that the subretinal fluid originates from the vitreous in eyes with retinal detachments and tears. Samuels [130] describes 19 eyes studied histologically that had melanomas of the choroid and minimal circumscribed detachments of the retina or detachments of the ora serrata. He believes that the source of the subretinal fluid is the engorged choroidal blood vessels at the base of the tumor.

NEMATODE ENDOPHTHALMITIS

A pathological diagnosis of endophthalmitis, pseudoglioma or Coats's disease is usually a descriptive, rather than an etiological, one. Wilder [131] made a histological search for nematode larvae in 46 eyes in which this diagnosis was made. Each eye was obtained from a different patient, and in the majority of instances the patients were children. In 24 specimens the nematode larvae or their residual hyaline capsules were found. In the remaining 22 specimens the pathological picture was so similar to that of eyes in which the worms were found that a probable diagnosis of nematode endophthalmitis was made. The characteristic lesion was an eosinophilic abscess with a center in which the cytoplasmic granules tended to become basophilic as a result of necrosis. Surrounding the abscesses were epithelioid cells, occasional giant cells and inflammatory granulation tissue infiltrated by eosinophils, lymphocytes and plasma cells. Eosinophilic abscesses were distributed on the under side of the retina, in retinal folds and in the vitreous. Scars, which undoubtedly marked the tracks of the larvae, passed from the inner layers of the choroid through the retina, interrupting Bruch's membrane and often forming a chorioretinal adhesion. This report is of great importance as another milestone in the advancing knowledge of the etiology of chorioretinitis and should stimulate other workers to make similar studies for the presence of nematodes in cases of uveitis of unknown cause.

METHODS OF EXAMINATION

Improvements in the slit lamp and biomicroscope by Haag-Streit and Zeiss-Opton have made binocular examination of the fundus with a slit of light a practical office procedure.[132] The shaft of light in the Haag-Streit instrument is brought to within 5 degrees of the visual axis by means of a permanently attached adjustable glass prism. On the Zeiss-Opton model the source of light may be placed between the objectives or at any angle up to 90 degrees. The refractive power of the eye may be neutralized either by a — 58 D. Hruby lens placed in front of the eye or by a Goldmann contact lens with a plano surface placed on the globe.[133]

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129. Godtfredsen, E.: Investigations into Hyaluronic Acid and Hyaluronidase in the Subretinal Fluid in Retinal Detachment, Brit. J. Ophth. **33**:721, 1949.

130. Samuels, B.: Detachment of the Retina in Early Sarcoma (Malignant Melanoma) of the Choroid, Arch. Ophth. **42**:620 (Nov.) 1949.

131. Wilder, H. C.: Nematode Endophthalmitis, Tr. Am. Acad. Ophth. **55**:99, 1950.

132. Littmann, H.: A New Slitlamp Apparatus, Am. J. Ophth. **33**:1863, 1950.

133. Hruby, K.: Slit Lamp Microscopy of the Posterior Section of the Eye with the New Preset Lens, Arch. Ophth. **43**:330 (Feb.) 1950. Goldmann, H.: Slitlamp Examination of the Vitreous and the Fundus, Brit. J. Ophth. **33**:242, 1949.

Correspondence

USE OF COATED LENSES IN RETINOSCOPY

To the Editor:—A note in this journal (Zugsmith, G. S.: Use of Coated Lenses in Retinoscopy, ARCH. OPHTH. **39:** 383-385 [March] 1948) claims advantages with the use of coated trial lenses, many of which seem reasonable.

The refractions of 100 patients were determined with the retinoscope, using both coated and uncoated lenses and trial case acceptance. It is stated that, especially with respect to the cylindric correction, "there was closer correlation between trial case acceptance and retinoscopic corrections with coated lenses. . . . However, more apparent than the statistical results was the ease with which retinoscopic examination was performed."

The statistical results are, however, far from apparent, since neither the coefficient of correlation nor the differences with their probabilities are given. Data on only 17 (said to be "representative") of the 100 cases are recorded. The values for the cylinders and spheres of the 32 eyes were analyzed by us by the method of paired differences (Fisher, R. A.: Statistical Methods for Research Workers, ed. 10, Edinburgh, Oliver and Boyd, Ltd., 1946, p. 121). For the cylinders, the averages of the differences between the coated or the uncoated lenses and the trial case acceptance are very small (0.03 and 0.04 D.), and neither is significant ($P = 0.5$ and 0.2). For the spheres, the averages of the differences are also small (0.11 and 0.08 D.), with probabilities of 0.2 and 0.3. If the 17 cases published are, as claimed, representative, there is no evidence that the differences are due to anything but chance.

It is unfortunate that clinical impressions, which are notoriously fallible, should take an apparent support from statistical analysis when this consists, as in the present case, merely in clothing the assertions in statistical terms. It is probable that the cause of coated lenses has been done a distinct disservice by the unsupported claims of this uncritical article.

Los Angeles College of Optometry.

MONROE J. HIRSCH, PH.D. and
FRANK W. WEYMOUTH, PH.D., Los Angeles.

Society Transactions

EDITED BY DR. W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Wilfred Fry, M.D., Chairman

M. Luther Kauffman, M.D., Clerk

Jan. 18, 1951

Biomicroscopy of the Zonule. DR. MILTON L. BERLINER, New York.

Dr. Berliner pointed out that much remains unknown about the zonule, not only its embryology and histology, but its dynamics and chemistry as well. Also, little is known of its relation to senile normal and pathologic states or its possible relation to cataract, glaucoma or retinal and choroidal separation. The reason for this is its hidden position and the impossibility of observing it with the biomicroscope except in pathologic conditions, in which the lens is displaced or shrunken or in which there is a coloboma of the iris.

He reviewed our present knowledge of zonular morphology, referring to the works of Egger, Goldsmith and Minsky.

He showed three principal areas of insertion on the lens—anterior, equatorial and posterior. The anterior insertion is situated farther axially than the posterior insertion. The fibers of the anterior leaf are stronger than those of the posterior leaf. This is because of the part played by the anterior fibers in accommodation, while the posterior fibers have only a supporting function. The posterior fibers are also much more delicate. In dislocated lenses the posterior fibers often remain attached, while the anterior ones are torn or broken.

The site of origin of the zonule fibers was discussed. The exact way in which the fibers originate from the flat portion of the ciliary body is still undecided. The various possibilities were discussed. Dr. Berliner expressed the opinion that its derivation from the epithelium or its underlying basement membrane seemed more logical than other suggestions which have been made.

Examination with high illumination is required, and the magnification should be at least 40 ×. All examinations must be by direct focal illumination. The beam should be directed first from one side and then from the other. The room should be dark and the observer partially dark adapted. Both the narrow and the wide beam should be employed. Specular reflection should be used for the superficial fibers, and attention to the area adjacent to the mirror zone helps in seeing the deeper fibers. The fibers appear as delicate threads, which glisten by specular reflection and occur in groups or bundles.

Recently Dr. Berliner has tried to examine the zonule in normal eyes or pathologic ones in which the lens was not dislocated. Better results were obtained by using contact lenses (Koeppe, Troncoso and Allen). The new Zeiss slit lamp is an additional help, as it eliminates the angle between illumination and observation. With the pupil widely dilated and the eye turned as far laterally as possible, the light can be directed behind the iris and the lens equator observed. With slight pressure on the sclera with a glass rod, one can see not only the zonule but also the tips of the ciliary processes. In this position, with the Hruby lens swung into position, the retina can be visualized up to the ora serrata. By this method a whole new field of study on the living eye is opened.

The zonule in certain hereditary and congenital anomalies, including coloboma of the lens, ectopia lentis, spherophakia and microphakia, was discussed. It was

suggested that all these conditions may be varying degrees of the same process, a congenital weakness or aplasia.

After an inflammatory process two types of alteration of the zonule are noticed: changes in the fibers themselves and the presence of deposits. Some fibers may be taut, others torn and others distorted; and there may be varying degrees of destruction. The deposits on the fibers consist of pigmented or whitish sheathing, making the fibers stand out in bold relief. The fibers are brittle, this condition accounting for the ease with which complicating cataracts can at times be removed intracapsularly.

Various alterations of the zonule resulting from trauma were discussed. The degree of damage varies with local conditions, depending on whether the lens is subluxated or luxated. Dr. Berliner pointed out the frequency with which the posterior fibers remain attached while the anterior fibers are broken or separated from the lens.

Dr. Berliner concluded his talk with a brief discussion of traumatic detachment of the zonular lamella. Undoubtedly, more frequent biomicroscopic examinations in cases of displaced lenses of hereditary, spontaneous or traumatic origin will reveal that separation of the zonule lamella is not as rare as was formerly thought.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Supplementary Edition of Motion Picture Reviews Now Available.—The Committee on Medical Motion Pictures of the American Medical Association has completed the first supplement to the second revised edition of the booklet entitled "Reviews of Medical Motion Pictures." This supplement contains 86 reviews of medical and health films reviewed in *The Journal of the American Medical Association* from Dec. 31, 1949 to Jan. 1, 1951. Each film has been indexed according to subject matter. The purpose of these reviews is to provide a brief description and an evaluation of motion pictures which are available to the medical profession.

Copies of this supplement are available upon request to:

The Committee on Medical Motion Pictures
American Medical Association
535 North Dearborn Street
Chicago 10, Ill.

New York Eye and Ear Infirmary.—The complete reorganization of Postgraduate courses at the New York Eye and Ear Infirmary has been accomplished, under the direction of Dr. Raymond E. Meek, chairman, and Dr. J. Gordon Cole, secretary-treasurer. Postgraduate courses for both eye and ear specialists are given throughout the year and are available for a limited number of students applying to the registrar at the Infirmary.

SOCIETY NEWS

Pennsylvania Academy of Ophthalmology and Otolaryngology.—The Pennsylvania Academy of Ophthalmology and Otolaryngology will hold its annual meeting at Galen Hall Hotel, Wernersville, Pa., May 3-6, 1951. Among the speakers scheduled to give one-hour formal papers are Dr. Bernard C. Gettes, Dr. Maurice H. Cottle, Dr. John M. McLean, Dr. Herbent T. Kelly, Dr. Theodore Walsh, Dr. Kenneth M. Day, Dr. Raymond Carhart, Dr. Harold G. Scheie, Dr. Paul M. Moore, Dr. Francis W. Davison, Dr. Peter C. Kronfeld, Dr. Dewey Katz, Dr. Edwin B. Dunphy and Dr. Campbell Moses.

In addition to the formal papers, 17 one-hour round table and panel discussions on important subjects will be presented.

Communications may be addressed to D. S. DeStio, M.D., secretary, 1006 Highland Bldg.

Ophthalmological Society of Vienna.—The Ophthalmological Society of Vienna announces that the University of Vienna is planning to honor the one-hundredth anniversary of the birth of Ernst Fuchs by an academic celebration on June 21, 1951, in which a marble relief of Ernst Fuchs, sculptured by J. Müller, will be unveiled in the hall of fame of the university.

The Viennese Medical Society will join with the Ophthalmological Society in a special session to celebrate this occasion on Friday, June 22. A detailed program of the academic ceremonies and of the list of papers to be presented at the scientific meeting will be published later.

The officers of the society are K. Lindner, president; C. Eyb, secretary; A. Pillat, vice president.

American Academy of Ophthalmology and Otolaryngology.—The 1951-1952 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of 10 months. Registrations must be completed before August 15. Detailed information and application forms may be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 100 First Avenue Building, Rochester, Minn.

PERSONAL NEWS

Appointment of Dr. Dan M. Gordon.—Announcement has been made of the appointment of Dr. Dan M. Gordon to the Advisory Council of the National Institute of Neurological Diseases and Blindness.

Dr. Harold F. Whalman Resumes Position.—Dr. Harold F. Whalman has resumed his position as professor and head of the department of ophthalmology in the College of Medical Evangelists, Los Angeles, after an extended illness.

Fellowship Award to Dr. Samuel Jiro Kimura.—Dr. Samuel Jiro Kimura, instructor in ophthalmology at the University of California Medical School in San Francisco, has been awarded a $30,000 five year fellowship by the John and Mary R. Markle Foundation of New York.

Dr. Kimura was graduated from the University of California School of Medicine in 1941 and at that time entered the Army Medical Corps. He served with the famous Japanese Battalion in combat in Italy, where he won the Purple Heart. After his certification by the American Board of Ophthalmology, Dr. Kimura was sent by the National Research Council to Nagasaki, Japan, to carry on research work in radiation cataract in the area affected by the atomic bomb.

At present Dr. Kimura is continuing his research work at the University of California Division of Ophthalmology.

Book Reviews

Eyes and Industry. By Hedwig S. Kuhn, M.D. Price, $8.50. Pp. 378, with 151 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1950.

The second edition of this book, published six years after the first edition, "Industrial Ophthalmology," represents an amplification of the large experience in the visual problems peculiar to industry as a result of studies during the war, and a more complete evaluation of screening tests of visual efficiency. Being situated in the highly industrialized community of Hammond, Ind., the author has had personal contact with the practical problems which arise when an attempt is made to select and place workers in jobs to which they are visually suited, to correct ocular defects, to provide adequate ocular protection and to treat injuries. The great variation of visual tasks in industry is emphasized by 151 illustrations, and the need for individualized selection of personnel, correction of defects and protection is reiterated frequently throughout the book.

The author was in close communication with the work of Joseph Tiffin and his group at Purdue University, concerned especially with mass visual screening by technicians trained in the use of the Ortho-Rater, from which "profiles" of visual standards were set up for each type of job after correlation had been made of visual efficiency and job efficiency. The exact details of these tests and correlations have not been described clearly in this book. In the appendix, Henry A. Imus, Office of Naval Research, presents important figures in the "test-retest" reliability of various screening devices (Ortho-Rater, Sight-Screener and Telebinocular) and routine clinical examination. It was found that the Ortho-Rater was as consistent as clinical examination, slightly more consistent than the Sight-Screener in most respects and much more consistent on "test-retest" work than the Telebinocular. It was found that the results of the individual tests on the Ortho-Rater, and to a slightly less extent on the Sight-Screener, could be correlated well with the individual clinical tests, and a model called the "Doctor's Ortho-Rater" has been produced.

Dr. Albert C. Snell has an excellent chapter on "Industrial Eye Injuries Caused by Solid Bodies," in which he terms the Berman Locator an "indispensable instrument for determining the presence and location of intraocular foreign bodies." Apparently, since this chapter was written, additional antibiotics (e. g., streptomycin, aureomycin and chloramphenicol [chloromycetin®]), different routes of administration and higher doses of penicillin have been recommended in the literature. Dr. Kuhn believes that "flash burns" can usually be alleviated completely within 12 to 18 hours by the proper use of local anesthetics, phenylephrine and cold compresses, and that some workers prolong the period of disability unnecessarily. She points out that the quantity of infrared rays or heat from various industrial processes necessary to produce cataract in humans is uncertain, leading to difficulty in compensation cases. With respect to chemical eye injuries, the importance of immediate and thorough irrigation of the eye is justly stressed. The author has gained the impression from large clinical experience that the instillation of hydrosulphosol® (a mixture of calcium polysulfides and thiosulfates) and the application of a pressure bandage produces rapider healing than methods used previously, but there is no clinical or experimental proof as yet that hydrosulphosol® is helpful.

There are also good chapters on eye protection (goggles), illumination and the blind in industry and a discussion of monocular aphakia in the worker. Somewhat surprising statistics are presented. Of 68 patients with monocular aphakia

and good vision in the other eye, 83 per cent "had no trouble whatsoever wearing their full correction"; 13 per cent had trouble for only a few months, and 4 per cent could not wear the full correction but one of these patients was able to wear a contact lens. In addition to being given encouragement, the patient is advised to cover the normal eye intermittently for relief of the diplopia and confusion during the first few months. In the appendix are included tables for calculation of visual efficiency for industrial compensation purposes, standards for goggles, a statement from the Joint Committee on Industrial Ophthalmology that "fluorescent light is not harmful to vision and should not cause discomfort if properly installed and used" and Cowan's statement against the widespread use of mildly tinted lenses for normally healthy eyes in ordinary sunlight.

The author strongly states that the approach to industrial problems should not be of the academic, or "ivory tower," variety. In warning against the "impractical, dogmatic attitudes of scientific sticklers," one must guard against the dogmatism of "experience" and uncontrolled clinical impression. The book is not designed as a monograph on statistical and research data, but, instead, brings together many practical facts needed for handling the problems of industrial ophthalmology.

Diagnosis and Treatment of Tumors of the Head and Neck (Not Including the Central Nervous System). By Grant E. Ward, M.D., D.Sc., and James W. Hendrick, M.D. Price, $15. Pp. 832, with 46 illustrations. The Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

Chapter 14 in this recent book on tumors of the head and neck has been written by Charles E. Iliff and concerns tumors of the eye and adnexa. It is an excellent résumé of the subject of extraocular and intraocular tumors and should be of use not only to ophthalmologists, but to general physicians as well, who frequently are first consulted by patients with lesions of this type.

The material is divided anatomically into tumors of the lid; tumors of the conjunctiva, cornea and caruncle; tumors of the iris, ciliary body, choroid and retina, and, finally, tumors of the orbit, optic nerve and lacrimal glands.

The manuscript is beautifully illustrated with photographs of patients and line drawings of operations. Treatment, both irradiation and surgical procedures, is outlined in detail.

The book can be recommended to all ophthalmologists for this chapter alone.

Ophthalmic Operations. By Seymour Phelps. Price, $9.50. Pp. 397, with 510 illustrations and 2 colored plates. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

This book is another in the rapidly growing list of volumes on ophthalmic surgery. It presents the experience of one surgeon but contains no bibliography. It gives very briefly the indications for operation, and only in selected instances are the complications discussed. In its format it is closer to an illustrated laboratory manual than to a standard textbook. In a terse, rather didactic style, various surgical procedures are described. Each operation is presented concisely and in the same manner. First the indications are listed; then the anesthesia is designated, the instruments are selected and, finally, the technic employed is briefly outlined. All these steps are amply illustrated, and the author is to be congratulated on the excellent photographs of the actual surgical procedures.

Many opinions are presented with which the reviewer is not in accord and which reflect thoughts on ophthalmic surgery somewhat different from those prevalent in this country. It is interesting that the author relies on silk and seldom, if ever, employs catgut, even in situations calling for buried sutures. No mention is made of the use of the erisiphake in cataract extraction, nor is the Kuhnt-

Szymanowski procedure for the correction of senile ectropion discussed. The author also, surprisingly enough, suggests the use of radon seeds or a radium applicator in cases of localized unilateral retinoblastoma.

A large amount of thought has been put into the construction of this book, but its scope it too limited to be of great value to the ophthalmic surgeon, and its text is not sufficiently detailed for adequate instruction of the student. It does, however, portray with great clarity the technics employed by the author.

Estrabismos y paralisis. By Jorge Malbrán, M.D. Pp. 680, with 221 illustrations. Editorial Oftalmológica Argentina, Buenos Aires, 1949.

The distinguished author, who, with Adrogué, published a volume on strabismus in 1938, presents in this well printed book a thorough analysis and study of the oculorotary muscles. The author's complete survey of the literature is evidenced by a bibliography of 412 references. The 19 chapters of this book begin with the anatomy and physiology of the ocular muscles, the sensory binocular mechanism and latent disturbances of the muscular equilibrium and end with seven sections on the ocular paralyses and a final chapter presenting illustrative clinical cases. There is an index to the chapter headings and contents, but no alphabetical index.

Malbrán from his vast experience, is convinced that the majority of cases of strabismus have a motor origin (anomalies of position, paralyses and pareses). In the portions dealing with the surgical technics employed in treatment, he describes only those procedures which he considers valuable and rational.

For the ophthalmologist who can read Spanish, this splendid book can be highly recommended as an up-to-date, authoritative treatise on strabismus.

Physiology of the Eye: Clinical Application. By Francis Heed Adler, M.A., M.D., F.A.C.S. Price, $12.50. Pp. 709, with 319 illustrations, including 2 in color. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1950.

About 20 years ago Adler, then instructor in physiology and ophthalmology at the University of Pennsylvania, conceived the idea of "a small text-book giving in as simple terms as possible the fundamental facts and the generally accepted theories of how the eye functions." Patterned on this idea, the "Clinical Physiology of the Eye" was published in 1933 (ARCH. OPHTH. **9**: 1018 [June] 1933) and became a companion piece to basic texts, such as Whitnall's "Anatomy of the Orbit" or Salzmann's "Histology." Even though the first and only edition of the "Clinical Physiology" became exhausted after a few years, several generations of neophytes in ophthalmology had the good fortune of being guided by this text during their first tottering steps in ophthalmology.

Adler's new "Physiology of the Eye" is not just a second edition of the "Clinical Physiology" of 1933. The two books are similar in purpose, general approach and style, but very dissimilar in factual contents and external appearance. The difference between the two books is a striking demonstration of the far-reaching changes that have occurred in the domain of ocular physiology during the last 20 years.

The new book, like its forerunner of 17 years ago, presupposes only an elementary knowledge of general human physiology and of anatomy of the eye. Wherever indicated and conveniently possible, the book lays its own foundation. For example, before presenting the metabolism of the cornea, Adler himself reviews the general principles of enzymatic breakdown of foodstuffs, instead of referring the student to a textbook on biochemistry. This method of presentation, maintained throughout the book, serves to link up ocular physiology with general science and to make the reader recognize general physiological principles in a great many reactions and responses of the human eye. Pursuing further the principle of integra-

tion of physiological knowledge, which is the obvious keynote of the book, Adler has included in it phenomena of pathologic physiology wherever their discussion rounds out or deepens the understanding of important, either physiological or disease processes.

The material is arranged in conventional sequence, that is, (1) protective apparatus, (2) vegetative functions of the eye and (3) physiology of vision. The chapters on the transparency and permeability of the cornea are largely based on the work and concepts of Cogan and Kinsey. Due consideration is given to the still controversial points in these authors' theory concerning the fluid movement in the cornea.

A remarkable, and probably unprecedented, degree of clarity is achieved in the chapters dealing with the aqueous humor and the intraocular pressure. The material, that is, the chemical data pertaining to the steady or the dynamic state, is chosen carefully from reliable sources and introduced in logical order. It adds up to a very strong case for the secretion-diffusion theory, as conceived and elaborated by Friedenwald and Kinsey and associates. By a similar process of systematic build-up, the intraocular pressure and its variations are shown to depend primarily on the osmotic pressure differences between aqueous and plasma, the local capillary blood pressure and the resistance to outflow. The author's intention of leading his readers toward relatively simple but realistic and workable concepts is well accomplished in these chapters dealing with the exchange of the eye.

The chapter on the physiology of the iris muscles has been enriched by a short pharmacological and a rather detailed pathological section, the latter dealing with typical lesions of the pupillary pathway. What might seem like a detour into the fields of pharmacology and neurology proves a means of rounding out the understanding of normal function. The theory of accommodation is presented in great detail, perhaps in order to give the reader some insight into ophthalmological thinking and speculation rather than for the practical value of the theory. The chapter on ocular circulation (placed between fluid exchange and ocular motility) is characterized by broad general foundation, out of which, almost imperceptibly, the specific features of ocular vascular dynamics are developed. A fairly detailed discussion of essential hypertension in man demonstrates the value of normal vascular dynamics for the understanding of vascular disease.

The comprehensiveness of the section on ocular motility is indicative of the author's special interest in this field. While a great deal of minute detail is offered, the reader is kept aware of the main purpose of the book, that is, the understanding of gross function. The highly practical section on motor anomalies and muscle operations will compensate the reader for his efforts at assimilating some of the more academic material presented in the preceding section. After a short chapter on the physics of light, the author turns to the physiology of vision, taking up first the objectively observable and measurable phenomena, that is, the photochemistry of the retina, the photic responses of lower animals and, finally, the electric phenomena associated with nerve conduction (the electroneurogram) and retinal activity (the electroretinogram). There follow two chapters dealing with the anatomical organization of retina and visual pathway. Having arrived at the area striata, the author defines his location by quoting Penfield's famous statement of the visual cortex "forming a station in the afferent stream of visual impulses on their way from peripheral sense organs to the level of consciousness." Here Adler introduces vision as a subjective conscious experience by describing the visual sensations elicited in conscious human beings by direct stimulation of the visual cortex. He then discusses the prevailing theories (Lashley, Adrain, Hoagland, Pitts and McCulloch) concerning higher brain function as related to visual sensations. From this highest, or final, level of visual manifestations Adler steps down to the retinal level and deals in the following chapters with the phenomena of adaptation and induction. Some readers will miss here a more systematic presentation of the general qualities of visual sensations. The absence of such a chapter is

particularly conspicuous in a book as replete with formulations of general principles as Adler's. The closing chapters concern themselves with visual acuity, color vision, binocular vision and entopic phenomena. The distribution of space in these chapters does not seem quite fair, color perception and binocular vision being the stepchildren.

In summary, the book is outstanding in lucidity and in maintaining a straight path through a maze of data and theory. In most places it strikes a happy medium between the old and the new. It is beautifully and most instructively illustrated. There is a good selection of key references at the end of each chapter. The book sets a high standard for the amount of physiological knowledge which should be the basis for the rational practice of ophthalmology. No other book contains that amount of physiological knowledge in such well organized and assimilable form. There can be no doubt that Adler's "Physiology" will vary materially and in many ways contribute to the progress of ophthalmology.

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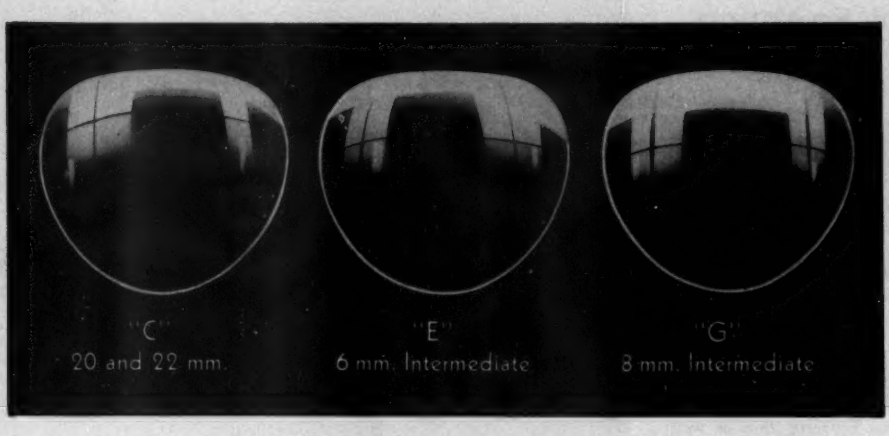

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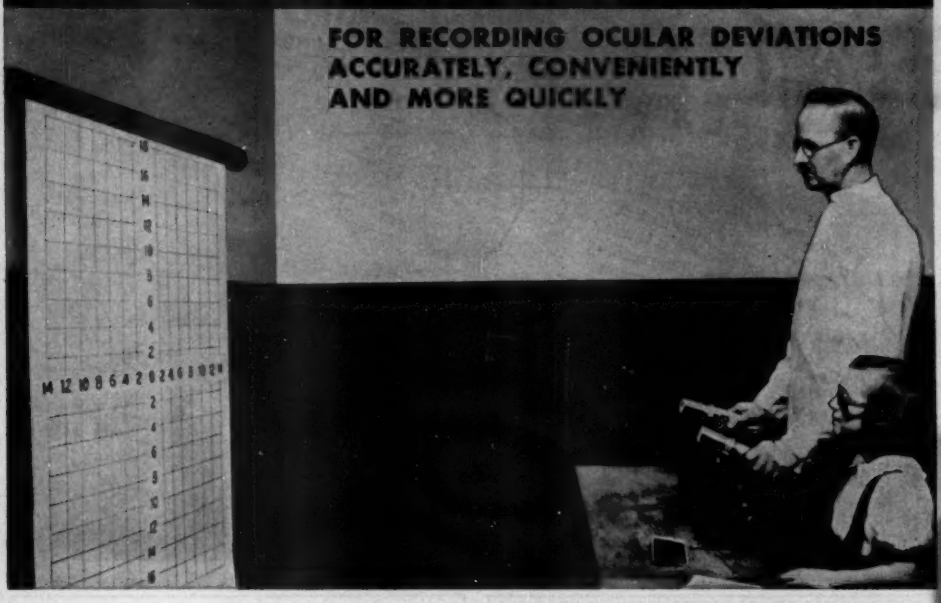

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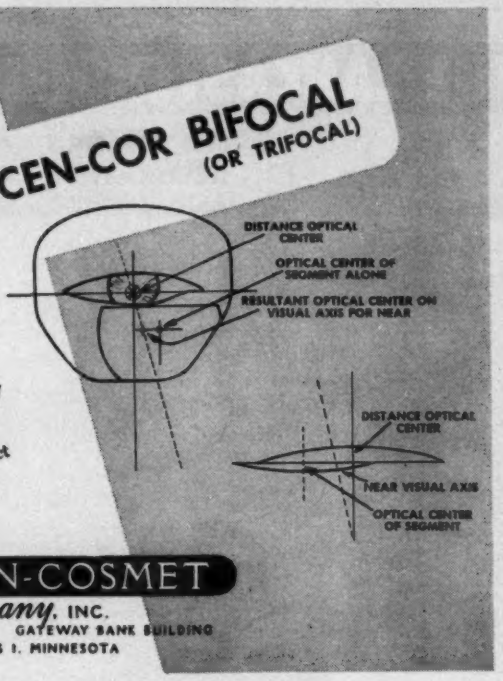
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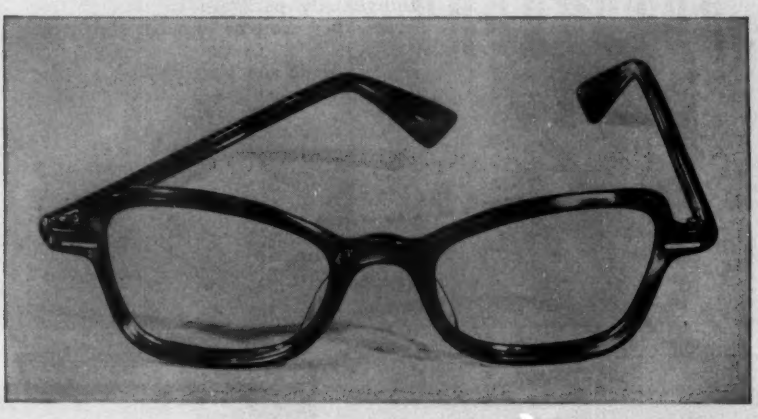

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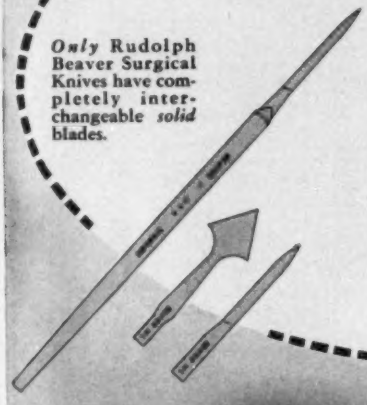

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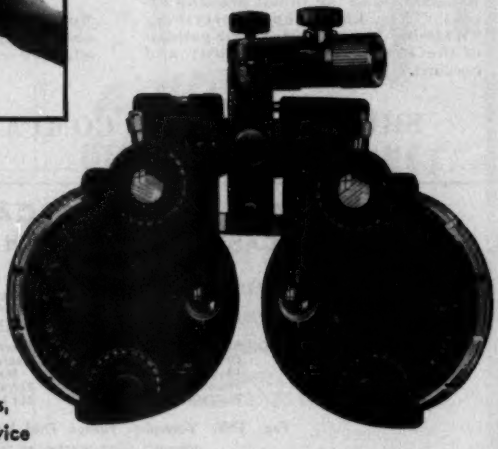

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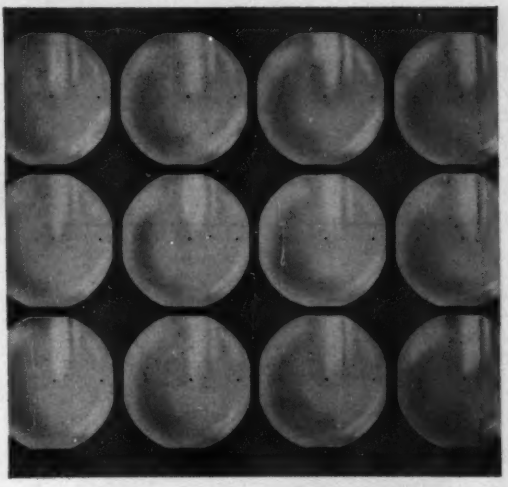

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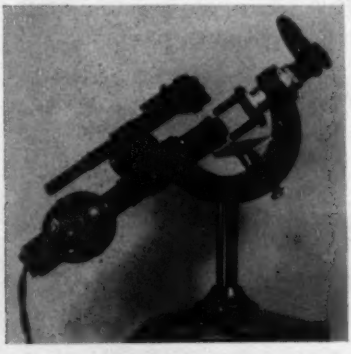

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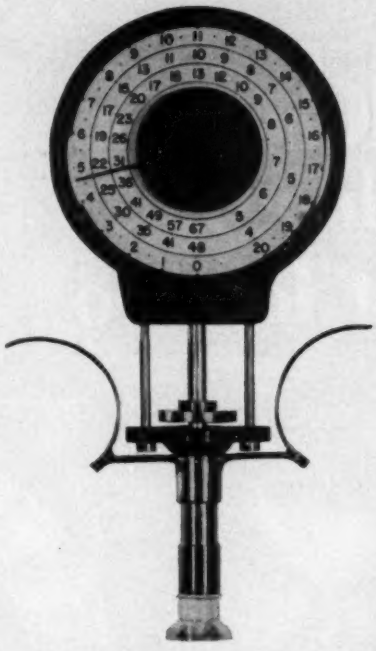

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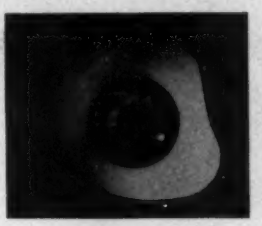

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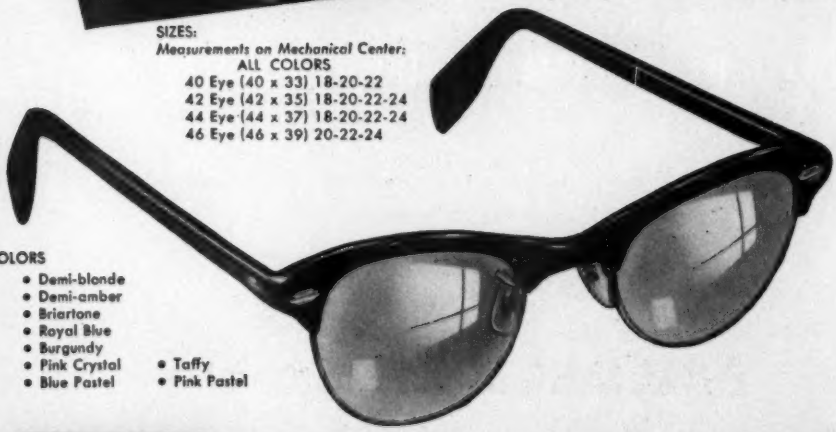

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